UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION	**2:17-MD-2789 (CCC) (LDW) (MDL 2789) and all member and related cases**
This Document Relates to: All Actions	**Judge Claire C. Cecchi**

REPORT & RECOMMENDATION OF SPECIAL MASTER ELLEN K. REISMAN REGARDING *DAUBERT* MOTIONS

TABLE OF CONTENTS

I. INTRODUCTION

The Judicial Panel on Multidistrict Litigation ("JPML") established this MDL 2789 proceeding in August 2017 to consolidate claims alleging personal injury and wrongful death resulting from the use of proton pump inhibitor drugs ("PPIs"). In Case Management Order ("CMO") No. 33, the Court created a process for bellwether selection, and in accordance with CMO No. 36, twenty plaintiffs were identified as those whose cases would be worked up as potential bellwethers.[1] In CMO No. 48, the Court selected six cases that were designated as the Bellwether Trial Cases and the parties have been preparing these cases for trial.[2] Trial in the first bellwether case, *Rieder*, is scheduled to begin on November 14, 2022, with trial in *Foster* scheduled on March 1, 2023, and trial in *Bales* scheduled on April 10, 2023.[3]

In CMO No. 50, amended by subsequent CMOs, including CMOs No. 75 and No. 76, the Court directed me to prepare Reports & Recommendations ("R&Rs") as to the parties' summary judgment motions, motions to exclude expert testimony under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*,[4] and certain other motions in

[1] CMO No. 33, ECF No. 513; CMO No. 36, ECF No. 548.
[2] CMO No. 48, ECF No. 665. The six cases selected as the Bellwether Trial Cases are *Freddy Bales*, No. 2:17-cv-06124; *David Foster*, No. 2:17-cv-02475; *Steve Kersch*, No. 2:18-cv-03159; *Kimberly Lee*, No. 2:17-cv-00212; *Diane Nelson*, No. 2:17-cv-13727; and *James Rieder*, No. 2:19-cv-00850.
[3] CMO No. 76, ECF No. 801.
[4] 509 U.S. 579 (1993).

the six Bellwether Trial Cases.[5] To facilitate the preparation of my R&Rs, I requested oral argument from the parties as to certain motions. On April 4 and 5, 2022, I held those oral arguments; the transcript of the April 4 oral arguments on the *Daubert* motions is attached hereto as Exhibit No. 1.[6]

The Plaintiffs' Steering Committee ("PSC") filed briefs and presented arguments on behalf of the individual plaintiffs. AstraZeneca Pharmaceuticals LP and AstraZeneca LP (collectively "AstraZeneca") are defendants in all six of the Bellwether Trial Cases, and Merck Sharp & Dohme Corporation is named as a defendant in the *Rieder* and *Kersch* cases.[7] Takeda Pharmaceuticals Company Limited, Takeda Pharmaceuticals America, Inc., Takeda Development Center Americas, Inc. f/k/a Takeda Global Research & Development Center, Inc., and Takeda Pharmaceuticals U.S.A., Inc. (collectively "Takeda") are defendants in *Bales* only.

The PSC moved to exclude testimony by certain AstraZeneca and Takeda experts:[8]

1. Dr. Robert Gibbons on behalf of AstraZeneca in all six Bellwether Trial Cases;

[5] *See* CMO No. 50, ECF No. 685; CMO No. 75, ECF No. 784; CMO No. 76.
[6] Oral Args., Apr. 4, 2022, attached as Ex. 1.
[7] For purposes of this R&R, "AstraZeneca" also includes Merck Sharp & Dohme Corporation for those two cases.
[8] Pls.' Omnibus *Daubert* Mot. to Exclude Defense Experts, ECF No. 702.

2. Dr. Jennifer A. Pinto-Martin on behalf of AstraZeneca in all six Bellwether Trial Cases;

3. Dr. Janice Lansita on behalf of AstraZeneca in all six Bellwether Trial Cases;

4. Dr. Marianne Mann on behalf of AstraZeneca in all six Bellwether Trial Cases;

5. Dr. Rajat Deo on behalf of AstraZeneca in the *Rieder* and *Bales* cases;

6. Dr. Jonathan Opraseuth on behalf of AstraZeneca in the *Lee* case;

7. Dr. Caren S. Palese on behalf of AstraZeneca in the *Rieder* case;

8. Dr. Leonard-Segal on behalf of Takeda in the *Bales* case;

9. Dr. Jerry Hardisty on behalf of Takeda in the *Bales* case; and

10. Dr. Richard Hansen on behalf of Takeda in the *Bales* case.

AstraZeneca moved to exclude testimony by certain plaintiffs' experts:

1. Dr. David Ross on behalf of the plaintiffs in all six Bellwether Trial Cases;[9]

2. Dr. Gilbert Moeckel on behalf of the plaintiffs in all six Bellwether Trial Cases;[10]

[9] AstraZeneca's Mot. to Exclude Op. Test. from Dr. David Ross Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 33 [hereinafter AstraZeneca's Mot. to Exclude Ross]. For ease of reference, this R&R will only cite to one of the parallel motions filed on the individual dockets of multiple Bellwether Trial Cases.

[10] AstraZeneca's Mot. to Exclude Op. Test. from Dr. Gilbert Moeckel Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 38 [hereinafter AstraZeneca's Mot. to Exclude Moeckel].

3. Dr. Burt Gerstman on behalf of the plaintiffs in all six Bellwether Trial Cases;[11]

4. Dr. Wajahat Mehal on behalf of the plaintiffs in the *Bales*, *Foster*, *Lee*, *Nelson*, and *Rieder* cases;[12]

5. Dr. Martin Wells on behalf of the plaintiffs in all six Bellwether Trial Cases;[13]

6. Dr. David Charytan on behalf of the plaintiff in the *Rieder* case;[14]

7. Dr. Derek Fine's case specific causation testimony on behalf of the plaintiff in the *Rieder* case;[15]

8. Dr. Jeffrey Silberzweig on behalf of the plaintiffs in the *Foster* and *Kersch* cases;[16]

9. Dr. David Powers on behalf of the plaintiffs in the *Bales* and *Lee* cases;[17] and

---

[11] AstraZeneca's Mot. to Exclude Op. Test. from Pls.' General Causation Experts Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 37 [hereinafter AstraZeneca's Mot. to Exclude Pls.' General Causation Experts].

[12] AstraZeneca's Mot. to Exclude General Causation Experts.

[13] AstraZeneca's Mot. to Exclude Op. Test. from Dr. Martin Wells Under Federal Rule of Evid. 702, *as filed in Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 34 [hereinafter AstraZeneca's Mot. to Exclude Wells].

[14] AstraZeneca's Mot. to Exclude Pls.' General Causation Experts.

[15] AstraZeneca's Mot. to Exclude Op. Test. From Pls.' Specific Causation Experts Under Federal Rule of Evid. 702, *as filed in Bales*, *Foster*, *Kersch*, *Lee*, *Nelson*, *& Rieder*, No. 2:19-cv-00850, ECF No. 35 [hereinafter AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts].

[16] AstraZeneca's Mot. to Exclude Pls.' General Causation Experts; AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts.

[17] AstraZeneca's Mot. to Exclude Pls.' General Causation Experts; AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts.

10. Dr. Richard Lafayette on behalf of the plaintiff in the *Nelson* case.[18]

AstraZeneca also moved to disqualify Dr. Gilbert Moeckel from testifying in the six Bellwether Trial Cases.[19]

Takeda moved to exclude the testimony by Dr. David Ross[20] and Dr. Gilbert Moeckel[21] in the *Bales* case. AstraZeneca and Takeda jointly moved to exclude the testimony of Dr. Martin Wells in the *Bales* case.[22]

On March 25, 2022, counsel for AstraZeneca, Takeda, and the PSC submitted a joint report withdrawing certain motions and narrowing the issues or waiving oral argument as to certain motions.[23] The PSC withdrew its motion to exclude the testimony of Dr. Pinto-Martin, and AstraZeneca withdrew its motion to exclude the testimony of Dr. Gerstman.[24] This R&R addresses certain of the parties' *Daubert* motions, where applicable as amended by the March 25, 2022 report. This R&R does not address experts Dr. Opraseuth, Dr. Hansen, Dr.

[18] AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts.
[19] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, *as filed in Bales, Foster, Kersch, Lee, Nelson, & Rieder*, No. 2:19-cv-00850, ECF No. 36.
[20] Takeda's Mot. to Exclude Test. of Dr. David Ross, No. 2:17-cv-06124, ECF No. 77.
[21] Takeda's Mot. to Exclude Expert Test. of Dr. Gilbert Moeckel, No. 2:17-cv-06124, ECF No. 80.
[22] Defs' Mot. to Exclude Op. Test. from Dr. Martin Wells Under Federal Rule of Evid. 702, No. 2:17-cv-06124, ECF No. 76.
[23] Joint Report to the Special Master Re *Daubert* Mot. Oral Args., attached as Ex. 2.
[24] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 1.

Hardisty, Dr. Powers, Dr. Silberzweig, Dr. Lafayette, and Dr. Leonard-Segal, all of whom are designated in cases other than *Rieder*.[25]

This R&R first reviews the legal standard set forth in Federal Rule of Evidence 702 and *Daubert* and the Third Circuit's application thereof. It then contains recommendations regarding *Daubert* motions made by the PSC, followed by recommendations regarding *Daubert* motions made by AstraZeneca and Takeda, as well as a recommendation regarding AstraZeneca's motion to disqualify Dr. Moeckel.

II. OVERVIEW OF RELEVANT LEGAL STANDARD

Federal Rule of Evidence 702 provides that:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

[25] I will address the *Daubert* motions to exclude the testimony of Dr. Opraseuth, Dr. Dr. Hansen, Dr. Hardisty, Dr. Powers, Dr. Silberzweig, and Dr. Lafayette in separate Report & Recommendations. With respect to Dr. Leonard-Segal, I submitted a Report & Recommendation on June 17, 2022, recommending that the PSC's *Daubert* motion be held in abeyance pending resolution of the PSC's motion to disqualify her. No. 2:17-cv-06124, ECF No. 114.

A district court serves a "gatekeeping" function under Rule 702 concerning expert testimony and must ensure that any expert testimony is both relevant and reliable before allowing its admission.[26] The ultimate goal of this analysis is to ensure that the trier of fact is presented only with reliable testimony that will help it understand the evidence or determine the relevant facts.[27] The burden of proof that the expert's testimony will be both reliable and relevant rests on the party offering the expert testimony.[28]

The Third Circuit applies Rule 702 and *Daubert* through a "trilogy of restrictions" on admission of expert testimony, examining the qualifications of the expert, the reliability of the expert's opinion, and the fit of the expert's opinion to the issues presented in the particular case.[29] First, the expert may be qualified through "a broad range of knowledge, skills, and training[.]"[30] Second, the expert's testimony must be reliable and based on the "methods and procedures of science" rather than on "subjective belief or unsupported speculation."[31] Third, the testimony must fit the particular case "as a precondition to admissibility,"

[26] *Daubert*, 509 U.S. at 589.
[27] *In re: Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 800 (3d Cir. 2017).
[28] *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Practices & Prods Litig.*, 509 F. Supp. 3d 116, 147-48 (D.N.J. 2020) (citing *Crowley v. Chait*, 322 F. Supp. 2d 530, 537 (D.N.J. 2004)).
[29] *Schneider ex rel. Estate of Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003).
[30] *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 741 (3d Cir. 1994).
[31] *Daubert*, 509 U.S. at 590.

demonstrated by a "valid scientific connection" between the testimony and the issues presented in a particular case.[32]

The Third Circuit has recognized that, in performing its critical gatekeeping function under *Daubert* with respect to expert testimony, a trial court must bear in mind "the preference for admissibility of the Federal Rules of Evidence" and avoid excluding expert evidence solely because the court does not think it is ultimately the most persuasive evidence.[33] This preference for admissibility offsets the risk that a trial judge may interpret the "amorphous" reliability standard too strictly.[34]

A. Qualifications

The Third Circuit reads the qualification requirement broadly and interprets it liberally.[35] To satisfy the qualification requirement, an expert must possess specialized knowledge in the area of testimony.[36] An expert may be qualified by a "broad range of knowledge, skills, and training[,]" including both academic credentials and practical experience.[37] This policy does not require that an expert possess the best formal or substantive qualifications, and more generalized qualifications are satisfactory.[38]

---

[32] *See id.* at 591-92; *Paoli*, 35 F.3d at 742-43.
[33] *See Paoli*, 35 F.3d at 750.
[34] *Id.*
[35] *Pineda v. Ford Motor Co.*, 520 F.3d 237, 244 (3d Cir. 2008).
[36] *Waldorf v. Shuta*, 142 F.3d 601, 625 (3d Cir. 1998).
[37] *Pineda*, 520 F.3d at 244 (quoting *Paoli*, 35 F.3d at 741).
[38] *See Pineda* at 244; *Paoli*, 35 F.3d at 741.

Courts have applied these standards to specific disciplines. Physicians, for example, do not need to be highly specialized in the area on which they are to testify or treat patients with the medical condition or symptom in question for their expert testimony to be admissible; the quality and depth of their qualifications goes to the credibility and weight to be accorded their testimony.[39] Physicians who are serving as experts, however, must demonstrate some minimal relevant knowledge and experience.[40] Similarly, biostatisticians are not required to be specialists in the subject matter to which they apply their statistical methodologies.[41] With respect to Food and Drug Administration ("FDA") experts, courts have ruled that their regulatory training and experience while at the agency, coupled with their other professional credentials, are sufficient to qualify them to testify on regulatory topics.[42]

---

[39] *See Paoli*, 35 F.3d at 753 ("We hold that Dr. Sherman, while arguably a relatively poor clinician and less than fully credible witness, qualifies as an expert.").

[40] *See Diaz v. Johnson Matthey, Inc.*, 893 F. Supp. 358, 372-73 (D.N.J. 1995) (excluding testimony of a pulmonologist who had never treated a patient with the particular respiratory condition at issue, was unfamiliar with the literature on the condition, and lacked any additional qualifications that would render the pulmonologist's testimony helpful in other ways).

[41] *See Hospira, Inc. v. Amneal Pharms., LLC*, 285 F. Supp. 3d 776, 811 (D. Del. 2018) (allowing a biostatistician to offer a statistical analysis of drug formulation because it fell "squarely within his realm of expertise[,]" even though he was not an expert on drug development).

[42] *Wolfe v. McNeil-PPC, Inc. (Wolfe I)*, 881 F. Supp. 2d 650, 658 (E.D. Pa. 2012); *Terry v. McNeil-PPC, Inc. (In re Tylenol (Acetaminophen) Mktg., Sales Practices, & Prods. Liab. Litig.) (Terry I)*, No. 2:12-cv-07263, 2016 U.S. Dist. LEXIS 99177, at *17 (E.D. Pa. July 28, 2016).

B. Reliability

The reliability inquiry looks at the scientific validity of the methodology underlying the expert's opinion.[43] An expert's opinion is reliable if it is "based on the 'methods and procedures of science' rather than on 'subjective belief or unsupported speculation'; the expert must have 'good grounds' for his or her belief."[44] The expert's testimony "must be derived by the scientific method" and "supported by appropriate validation -- *i.e.*, 'good grounds,' based on what is known."[45]

Both the methodology and its application must be reliable for the testimony to be admissible.[46] To determine the reliability of expert testimony, the court must make a "preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue."[47] Pursuant to *Daubert* and its Third Circuit progeny, the trial court should consider eight key factors when making this determination:

> "(1) whether a method consists of a testable hypothesis; (2) whether the method has been subject to peer review; (3) the known or potential rate of error; (4) the existence and maintenance of standards controlling the technique's operation; (5) whether the method is generally accepted; (6) the relationship of the technique to methods which have been established to be reliable; (7) the qualifications of the expert witness

[43] *See Paoli*, 35 F.3d at 742; *Schneider*, 320 F.3d at 404.
[44] *Paoli*, 35 F.3d at 742.
[45] *Daubert*, 509 U.S. at 590.
[46] *In re: Zoloft*, 858 F.3d at 792.
[47] *Daubert*, 509 U.S. at 592.

> testifying based on the methodology; and (8) the non-judicial uses to which the method has been put."[48]

This list of factors is non-exhaustive and may not be applicable in every case.[49]

An expert must, at a minimum, identify the methodology or procedures used or explain how the conclusions were reached by that expert.[50] The reliability standard requires some showing of methodological soundness and consistency. Additionally, the data and materials considered by the expert must be available.[51] Both the methodology and its application must be reliable for the testimony to be admissible.[52] If any step in the expert's methodology or analysis is unreliable, the whole testimony based on that analysis is inadmissible.[53] Further, if the expert chooses to employ a non-standard methodology or applies the chosen methodology unevenly, the expert must thoroughly explain the decision to do so.[54]

---

[48] *Elcock v. Kmart Corp.*, 233 F.3d 734, 745-46 (3d Cir. 2000) (citing *Paoli*, 35 F.3d at 742 n.8).

[49] *See Kannankeril v. Terminix Int'l*, 128 F.3d 802, 806-07 (3d Cir. 1997); *see also Paoli*, 35 F.3d at 742 ("*Daubert* . . . indicates that the inquiry as to whether a particular scientific technique or method is reliable is a flexible one.").

[50] *See Sikkelee v. Precision Airmotive Corp.*, 522 F. Supp. 3d 120, 158 (M.D. Pa. 2021) ("[R]elying on an expert's *ipse dixit* alone does not ensure that reliable principles and methods were used. Because [the expert] provides nothing else, the Court cannot allow the jury to hear this testimony."); *Buzzerd v. Flagship Carwash of Port St. Lucie Inc.*, 669 F. Supp. 2d 514 (M.D. Pa. 2009) (a mechanic's failure to articulate any methodology by which to assess carbon monoxide accumulation rendered the method untestable).

[51] *In re Johnson & Johnson Talcum Powder*, 509 F. Supp. 3d at 155.

[52] *In re: Zoloft*, 858 F.3d at 795-96.

[53] *Id.* at 800.

[54] *In re: Zoloft*, 858 F.3d at 797-99.

The reliability prong is satisfied so long as the expert's opinion "reliably flow[s] from th[e] methodology and the facts at issue[.]"[55] The party seeking to admit expert testimony must prove only that the testimony is reliable, not prove to the court by a preponderance of the evidence that the expert's conclusion is correct.[56] The opinion does not need to have the strongest evidentiary foundation or be "supported by the best methodology or unassailable research" to survive a *Daubert* motion.[57] Nor must it rely on published, peer-reviewed studies, although such reliance is one indicium of reliability.[58] Surface-level flaws relating to methodology may be reserved for cross-examination, though "'there will be occasions when the proffered [expert evidence] is so flawed' that it is 'completely unhelpful to the trier of fact' and 'its probative value is substantially outweighed by its prejudicial effect.'"[59] In short, "the reliability requirement must not be used as a tool by which the court excludes all questionably reliable evidence."[60]

---

[55] *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 152 (3d Cir. 1999).
[56] *In re TMI Litig.*, 193 F.3d 613, 665 (3d Cir. 1999).
[57] *Id.*
[58] *See Heller*, 167 F.3d at 154; *In re TMI Litig.*, 193 F.3d at 663-64.
[59] *Bruno v. Buzzuto's, Inc.*, No. 3:09-cv-874, 2015 U.S. Dist. LEXIS 156339, at *140 (M.D. Pa. Nov. 19, 2015) (quoting *Malletier v. Dooney & Bourke, Inc.*, 525 F. Supp. 2d 558, 563 (S.D.N.Y. 2007)).
[60] *Paoli*, 35 F.3d at 744 (quoting *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829 (3d Cir. 1990).

Exclusion is appropriate only if the flaw in the methodology is "large enough that the expert lacks 'good grounds' for his or her conclusions."[61] Even if the judge believes "there are better grounds for some alternative conclusion," and there are some flaws in the scientist's methods, if there are "good grounds" for the expert's conclusion, it should be admitted.[62] The testimony may be "tested by the adversary process—competing expert testimony and active cross-examination—rather than excluded from jurors' scrutiny for fear that they will not grasp its complexities or satisfactorily weigh its inadequacies."[63]

With respect to medical experts, a physician's highly specialized academic and professional qualifications in the area on which that expert is to testify favor a finding of reliability.[64] Where a medical expert opines with respect to causation of a plaintiff's illness, the "medical expert's causation conclusion should not be

---

[61] *See Paoli*, 35 F.3d at 746; *Hoffeditz v. AM General*, No. 09-0257, 2017 U.S. Dist. LEXIS 123493, at *13-14 (D.N.J. Aug. 4, 2017) (noting that studies relied upon by challenged expert were subject to legitimate criticism from opposing party's experts but finding that such contradictions were appropriately addressed through cross-examination, not exclusion).

[62] *See Paoli*, 35 F.3d at 746; *Heller*, 167 F.3d at 153.

[63] *United States v. Mitchell*, 365 F.3d 215, 244 (3d Cir. 2004) (citing *Ruiz-Troche v. Pepsi Cola Bottling Co.*, 161 F.3d 77, 85 (1st Cir. 1998)); *Daubert*, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence."); *see also Heller*, 167 F.3d at 152.

[64] *See Schneider*, 320 F.3d at 407; *see also Keller v. Feasterville Fam. Health Care Ctr.*, 557 F. Supp. 2d 671, 677 (E.D. Pa. 2008) (admitting expert testimony about Alzheimer's Disease when the testifying physician was a well-respected expert in the field of neurodegenerative diseases).

excluded because he or she has failed to rule out every possible alternative cause of a plaintiff's illness."[65]

Courts have similarly found FDA regulatory expert testimony reliable when FDA experts rely on and apply the same methods used in their work at FDA with regard to regulation of drug approval and labeling.[66] Indeed, with regard to FDA experts testifying on regulatory issues, courts have found their experience at the agency to be particularly valuable, especially when coupled with additional industry or academic experience.[67] Questions regarding an FDA regulatory expert's methodology as to opinions on regulatory issues go to weight, not admissibility.[68]

---

[65] *See Heller*, 167 F.3d at 156; *see also Paoli*, 35 F.3d at 758-60 (applying flexible reliability standard and reversing district court's exclusion of physician testimony on differential diagnosis based solely on review of patient's medical records).

[66] In *Terry v. McNeil-PPC, Inc. (In re Tylenol (Acetaminophen) Mktg., Sales Practices, & Prods. Liab. Litig.) (Terry II)*, No. 2:12-cv-07263, 2016 U.S. Dist. LEXIS 117594, at *20 (E.D. Pa. Aug. 31, 2016), for example, the court found that any questions regarding the FDA expert's methodology went to weight, not admissibility. ("By all accounts, Dr. Jones' actual methods—reviewing and deciphering the information contained in documents provided her based on her professional experience—are reliable ways of reaching opinions about industry standards and the use of AERs."); *see also Johns v. CR Bard (In re Davol, Inc./C.R. Bard, Inc., Polypropylene Hernia Mesh Prods. Liab. Litig.)*, No. 2:18-cv-01509, 2021 U.S. Dist. LEXIS 143187, at *436 (S.D. Ohio Aug. 1, 2021) (stating that an expert's opinions were sufficiently reliable where her methodology was the one she was trained to use at the FDA); *Lemmon v. Wyeth. LLC*, No. 4:04-cv-01302, 2012 U.S. Dist. LEXIS 95924, at *27 (E.D. Mo. July 11, 2012) (admitting expert testimony regarding the drug approval process and analysis of the adequacy of the labeling because it was based upon specialized knowledge of the regulatory procedures, pharmaceutical labeling, and FDA standards and practice).

[67] *See Wolfe I*, 881 F. Supp. 2d at 650; *Terry I*, 2016 U.S. Dist. LEXIS 99177, at *4.

[68] *See, e.g., Terry II*, 2016 U.S. Dist. LEXIS 117594, at *20.

C. Fit

Expert testimony must fit the particular case and help the trier of fact understand the evidence or determine a fact in issue. This fit requirement speaks to the relevance of the expert opinion. "[A] valid scientific connection to the pertinent inquiry [is] a precondition to admissibility."[69] The standard is "not that high" but is "higher than bare relevance."[70] Even if the opinion is reliable, "scientific validity for one purpose is not necessarily scientific validity for other, unrelated purposes."[71] Expert testimony may fit even though it does not directly relate to the main legal issue. Scientific or medical expert testimony is not inherently unhelpful or confusing for the trier of fact simply because it is complex.[72]

III. PLAINTIFFS' MOTIONS

A. Dr. Marianne Mann[73]

AstraZeneca seeks to offer expert testimony by Dr. Marianne Mann on the adequacy of the warnings provided by AstraZeneca for Nexium with regard to renal

---

[69] *Daubert*, 509 U.S. at 592.
[70] *Paoli*, 35 F.3d at 745.
[71] *Daubert*, 509 U.S. at 591.
[72] *Keller*, 557 F. Supp. 2d at 679.
[73] As I disclosed during oral arguments, I worked with Dr. Mann years ago when I was a partner at Arnold & Porter and was representing American Home Products Inc. and Wyeth Pharmaceuticals in connection with the Diet Drug Litigation. Oral Args. 8:11-17, Apr. 4, 2022 ("One thing . . . I wanted to raise just in the way of full disclosures upfront . . . I don't know any of these experts personally except one who I did meet years ago, somewhere between 15 and 20 years ago, and that's [Marianne] Mann, and I think I had one meeting with her in connection with a case I was working on at the time.").

impairment and the appropriateness of FDA's decisions regarding the Nexium labeling. The PSC's motion to exclude Dr. Mann's opinion testimony rests upon two of the three criteria applied in the Third Circuit: qualifications and reliability. Specifically, the PSC argues that Dr. Mann is "unqualified to render an opinion on the causal association between PPIs and kidney injury" and that her testimony is unreliable because she lacks basic knowledge of FDA regulations and has not independently reviewed source data, instead relying on summaries prepared by FDA and the New Drug Application ("NDA") sponsor.[74] For the reasons discussed below, I recommend that this motion be denied.

1. Qualifications

Dr. Mann received an M.D. from the Medical College of Pennsylvania, completed her residency in internal medicine at Albert Einstein Medical Center and the University of Connecticut Health Center, and completed a fellowship in pulmonary and critical care medicine at the University of Connecticut Health Center.[75] She is currently board-certified in internal medicine and was previously board-certified in pulmonary care medicine and critical care medicine.[76]

[74] PSC's Mem. in Supp. of Pls.' Omnibus *Daubert* Mot. to Exclude Defense Experts 10-13, ECF No. 703 [hereinafter PSC's Omnibus Mem.].
[75] PSC's Omnibus Mem., Ex. 1 [hereinafter Mann Expert Report] at 1, ECF No. 703-1.
[76] Mann Expert Report, App. A.

Prior to joining FDA in 1994, Dr. Mann was a practicing physician with a specialty in pulmonary care from 1992-1994 and was a volunteer staff pulmonologist at National Naval Medical Center from 1994-2004. From 1994-2003, she held three positions at FDA: Medical Officer in the Division of Antiviral Drug Products/Division of Special Pathogens and Immunologic Drug Products, Deputy Director of the Division of Reproductive and Urologic Drug Products, and Deputy Director of the Division of Pulmonary and Allergy Drug Products.[77]

Dr. Mann's work at FDA included: reviewing clinical data and making approval recommendations for Investigational New Drug Applications ("INDs") and NDAs; participating in decisions on whether to put a study on hold; leading labeling discussions both with NDA sponsors and within the agency and addressing labeling changes; and managing safety issues that arose with products in both the pre-approval phase and during post-marketing experience. Dr. Mann summarizes her experience as follows: "[i]n total, I have had nine years of FDA experience in three different review divisions, including experience making final regulatory decisions, many of which concerned safety, about a wide variety of medications."[78] Dr. Mann received awards in recognition of her work at FDA, including: DHHS Secretary's Award for Distinguished Service, FDA Award of Merit, two FDA

[77] Mann Expert Report, App. A.
[78] Mann Expert Report 2.

Commendable Service Awards, and the Center for Drug Evaluation and Research's ("CDER") Excellence in Communication Award.[79]

From 2003-2004, Dr. Mann served as Branch Chief in the Respiratory Disease Branch Division of Microbiology and Infectious Disease at the National Institute of Health ("NIH") and since then has been a private consultant working on clinical and regulatory drug development.[80]

The PSC does not challenge Dr. Mann's qualifications generally. Instead, the PSC argues that Dr. Mann is not qualified to offer opinions on medical causation – whether and to what extent PPIs cause renal impairment. This argument is contrary to both the facts and the law.

First, AstraZeneca has made clear that it is not offering Dr. Mann as a medical causation expert. This appears consistent with her report, which focuses on regulatory history, regulatory decision-making, and the use of clinical and post-marketing surveillance data to inform labeling decisions. To support her opinions on these topics, Dr. Mann necessarily needed to review, analyze, and interpret data pertinent to whether and to what extent there is an association between PPI use and renal impairments. For example, she considers whether there were data sufficient, in her opinion as a former FDA officer, to constitute a signal of an association and/or to warrant a labeling change.

[79] Mann Expert Report, App. A.
[80] Mann Expert Report 2.

Dr. Mann is trained in internal medicine and, while at FDA, reviewed and analyzed pre-clinical and clinical trial data, adverse event data, and product labeling.[81] The fact that she is not holding herself out as an expert in nephrology does not mean that she is incapable of providing expert opinions about the data related to the association, if any, between PPI use and renal impairment and what, if anything, those data mean for labeling decisions. Review of data to assess risk and potential association is what senior FDA pharmaceutical regulators such as Dr. Mann do. Even if Dr. Mann had been offered to give testimony as to general medical causation in this case, she would be sufficiently qualified to do so under the liberal Third Circuit standard.

The PSC takes a few statements made at Dr. Mann's deposition out of context to attack her qualifications. First, she testified that she did not know specifically how long chronic kidney disease ("CKD") takes to develop, but knew it was a long process.[82] The PSC argues that this statement alone renders her "unqualified to give an expert medical opinion on whether a drug is associated with chronic kidney disease."[83] Perhaps if she were being offered to testify as to specific causation, her lack of specific knowledge would be a cause for concern, although even that is doubtful under the liberal Third Circuit standard.[84] It is certainly not an obstacle to her testimony here,

[81] Mann Expert Report 1.
[82] PSC's Omnibus Mem., Ex. 2 at 123:3-14 [hereinafter Mann Dep.], ECF No. 703-2.
[83] PSC's Omnibus Mem. 11.
[84] *See Wolfe v. McNeil-PPC, Inc. (Wolfe II)*, No. 07-348, 2011 U.S. Dist. LEXIS 47710, at *13 (E.D. Pa. May 3, 2011).

where she is being proffered to testify about data analysis concerning the potential association of PPIs with renal impairment from a regulatory perspective.[85]

Similarly, the PSC's citation of a statement in Dr. Mann's deposition that it is not her area of expertise to make individual case specific assessments of causation has no bearing on her qualification to testify as a regulatory expert. She is not being offered by AstraZeneca as a case specific causation expert.

2. Reliability

The PSC further argues that Dr. Mann's testimony is not reliable. First, the PSC argues that Dr. Mann "lacks basic knowledge of the regulations on which she claims to be an expert."[86] For this proposition, the PSC cites one response to a question in Dr. Mann's deposition in which she says that she has not reviewed enough adverse reaction sections of product labeling to say whether a company is permitted to add more detail to them. This one sentence, taken out of context, ignores her nine years of experience at FDA working on labeling and safety issues for multiple products. In context, the sentence appears to reflect a "thinking out loud" approach to a very specific question. She later went on to say that "[she doesn't] think being . . . in the adverse reactions section precludes adding slight

[85] *Lemmon*, 2012 U.S. Dist. LEXIS 95924, at *27 (finding that expert testimony regarding the drug approval process and analysis of the adequacy of product labeling was admissible because it was based upon specialized knowledge of the regulatory procedures, pharmaceutical labeling, and FDA standards and practices).
[86] PSC's Omnibus Mem. 12.

additional detail at times."[87] If the PSC believes that this point is relevant to any issue at trial, she can be cross-examined about it, but it hardly forms a basis to exclude her testimony.

Second, the PSC argues that because some of the materials Dr. Mann reviewed were summaries prepared by AstraZeneca or regulatory agencies, her methodology is unreliable. In support of this argument, the PSC points to several data points that it claims were excluded by AstraZeneca from its submission to the European Medicines Agency's Pharmacovigilance Risk Assessment Committee ("PRAC"), which Dr. Mann reviewed and about which she offered opinions.[88] More generally, the PSC criticizes her reliance on internal FDA reports – a type of document with which, as a former FDA officer, she has significant familiarity – because she could not say what information had been omitted from them. If the PSC's position is that no expert can ever rely on an agency report, a summary of data, or even a published article without going back and looking at all the source data, that is an extreme position that does not reflect the state of the law in the Third Circuit. To the extent the PSC wants to highlight any limits on the scope of data that Dr. Mann reviewed, the PSC may do so through cross-examination.

[87] Mann Dep. 112:13-16.
[88] PSC's Omnibus Mem. 13-15.

Finally, the PSC asserts that Dr. Mann's finding that AstraZeneca's conduct and certain labeling decisions were reasonable should be excluded because she "offers no yardstick by which her opinions . . . can be verified, tested and measured."[89] Again, that is not the law as to reliability of expert regulatory opinions. To the contrary, courts have found testimony of FDA regulatory experts to be reliable when the expert applies the same methodology used in the expert's work at FDA.[90]

3. Fit

The PSC does not challenge the fit of Dr. Mann's testimony, and there is no basis in the record to question the fit of her testimony.

B. Dr. Janice Lansita

AstraZeneca seeks to offer the testimony of toxicologist Dr. Janice Lansita, who opines that the "esomeprazole bridging studies met the criteria and requirements outlined in FDA guidance on new stereoisomers (1992) as referenced by FDA in the esomeprazole Pre-IND meeting minutes (1997)."[91] Dr. Lansita also stated in her report that the scientific principles for the bridging studies and toxicology study designs have not materially changed, and thus omeprazole and esomeprazole would

[89] PSC's Omnibus Mem. 18.
[90] *See, e.g.*, *Terry II*, 2016 U.S. Dist. LEXIS 117594, at *20; *Johns*, 2021 U.S. Dist. LEXIS 143187, at *436; *Lemmon*, 2012 U.S. Dist. LEXIS 95924, at *27.
[91] PSC's Omnibus Mem., Ex. 13 [hereinafter Lansita Expert Report] at 1, ECF No. 703-13.

likely be approved by FDA today.[92] Her report also included a sentence regarding the cost of developing a drug from discovery to marketing.[93] The PSC moved to exclude Dr. Lansita's testimony and asserts that Dr. Lansita is not qualified to opine on chronic progressive nephropathy ("CPN") and whether CPN is relevant to humans; Dr. Lansita is not qualified to opine on the cost of developing esomeprazole and/or the cost of drug development generally; and Dr. Lansita cannot provide a reliable opinion on whether the FDA would likely approve Prilosec or Nexium today.[94]

AstraZeneca subsequently stipulated that it does not oppose the PSC's motion "[t]o the extent Plaintiffs seek to prevent Dr. Lansita from offering an opinion on the pathological criterion or significance of [CPN] to humans"[95] and that it does not oppose the PSC's motion "[t]o the extent Plaintiffs seek to prevent Dr. Lansita from offering an opinion on the historical cost of bringing Prilosec or Nexium to market[.]"[96]

For the reasons set forth below, I recommend that the Court grant the PSC's motion in part and deny it in part. I recommend that:

- the PSC's motion be granted to the extent it seeks to prevent Dr. Lansita from offering an opinion on the pathological criterion or significance of CPN to humans, per the stipulation by AstraZeneca, and that it be

[92] Lansita Expert Report 14.
[93] Lansita Expert Report 1.
[94] PSC's Omnibus Mem. 43.
[95] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 6.
[96] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 7.

denied to the extent it otherwise seeks to prevent Dr. Lansita from offering her opinion on the nonclinical studies she reviewed;

- the PSC's motion be granted to the extent it seeks to prevent Dr. Lansita from offering on opinion on the historical cost of bringing Nexium or Prilosec to market, per the stipulation by AstraZeneca;
- the PSC's motion be granted to the extent it seeks to prevent Dr. Lansita from offering an opinion on the cost of bringing a drug to market generally;
- the PSC's motion be granted to the extent that it seeks to prevent Dr. Lansita from offering an opinion on whether PPIs would be approved by FDA today, but that it be denied to the extent it seeks to bar Dr. Lansita from opining on the sufficiency of the nonclinical studies to support FDA approval; and
- the PSC's motion be otherwise denied.

1. Qualifications

Dr. Lansita is a board-certified regulatory toxicologist with a B.A. in Biochemistry from Barnard College of Columbia University and a Ph.D. in Toxicology from the Massachusetts Institute of Technology ("MIT"). She worked as a regulatory toxicologist at Biogen, where she "learned to evaluate the toxicology of

novel drugs for first-in-human clinical trials."[97] From 2009-2014, Dr. Lansita worked as a Pharmacologist/Toxicologist for FDA in the CDER Division of Special Pathogen and Transplant Products where she "reviewed numerous … drug applications to determine if the nonclinical data were adequate to support drug safety in patients."[98] From 2012-2014, she served as Co-Chair of the CDER Pharmacology/Toxicology Coordinating Committee Nonclinical Biologics Subcommittee, where she was responsible for "leading discussions relevant to the nonclinical review of biologics for a group of ~35 pharmacology/toxicology reviewers across Divisions in CDER[.]"[99] Dr. Lansita estimates that she reviewed over one hundred drug applications to determine whether the nonclinical data, including laboratory and animal studies, were adequate to support drug safety in patients, and if not, what additional nonclinical studies should be performed.[100] Since she left FDA in 2014, Dr. Lansita has "worked with numerous start-up, pharmaceutical, and biotechnology companies (>60) to provide advice on toxicology studies, design toxicology studies, oversee the conduct of toxicology studies at contract research organizations (CRO), analyze and interpret the data from these studies, and use these data to evaluate the nonclinical safety of new drugs for clinical development."[101]

[97] Lansita Expert Report 1.
[98] Lansita Expert Report 1.
[99] Lansita Expert Report, App. C, 3.
[100] Lansita Expert Report 1.
[101] Lansita Expert Report 1.

As noted above, AstraZeneca has conceded that it does not oppose the PSC's motion to exclude Dr. Lansita from offering an opinion on the pathological criterion or significance of CPN to humans, and that it does not oppose the PSC's motion to exclude Dr. Lansita from offering an opinion on the historical cost of bringing Nexium or Prilosec to market.[102] The PSC challenges Dr. Lansita's qualifications on other grounds.

First, the PSC argues that Dr. Lansita is not qualified to testify about her evaluation of the nonclinical studies she reviewed and her interpretation of the results of those studies, including their discussion of CPN, because she is not an expert on kidney disease and relies upon the testimony of another defense expert regarding the pathology of CPN.[103] I believe that Dr. Lansita's work at FDA and in the private sector as a toxicology expert are sufficient for her to be qualified to opine on the results of the nonclinical studies she reviewed.[104] To the extent the PSC seeks to argue that Dr. Lansita's opinion should be given less weight because she is not a kidney disease expert, the PSC can do so through cross-examination at trial.

---

[102] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶¶ 6, 7.
[103] PSC's Omnibus Mem. 44.
[104] I note that the PSC's position is somewhat inconsistent with the position of the PSC's counsel at oral argument, who noted that plaintiffs' expert Dr. Ross was qualified to opine on case reports, adverse event reports, and other evidence relevant to the review of a warning in a drug label, as that is often done at FDA by internal medicine doctors, not specialists such as cardiologists or nephrologists. Oral Args. 91:21-92:15, Apr. 4, 2022 ("they are not specifically limited to the fields that they may have been trained in and specialized in.").

Second, the PSC challenges Dr. Lansita's qualification to opine on the cost of bringing a drug to market generally, as well as with respect to Nexium and Prilosec specifically. Dr. Lansita acknowledged that she is not able to speak to how much it cost to bring Nexium or Prilosec to market.[105] AstraZeneca does not oppose the PSC's motion to exclude Dr. Lansita from testifying regarding the historical cost of bringing Nexium or Prilosec to market,[106] leaving only the question of whether she is qualified to offer an opinion as to the cost of bringing a drug to market generally. AstraZeneca argues that Dr. Lansita is qualified to opine on the cost of bringing a drug to market generally based on her work at FDA, as well as her work in private practice before and after her time at FDA, and her reliance on a report from PhRMA, a pharmaceutical industry trade association.[107] The record, however, reflects that Dr. Lansita's experience at FDA was, and in private practice was and is, focused on nonclinical data and studies. There is nothing in the record to suggest, and AstraZeneca does not argue, that Dr. Lansita has experience or training in the costs

[105] PSC's Omnibus Mem., Ex. 14 [hereinafter Lansita Dep.] at 84:13-21, ECF No. 703-14.

[106] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 7.

[107] AstraZeneca's Mem. of Law in Opp'n to Pls.' Omnibus *Daubert* Mot. to Exclude Defense Experts 34-35 [hereinafter AstraZeneca's Opp'n to PSC's Omnibus Mem.] ECF No. 734. "PhRMA represents the nation's leading biopharmaceutical research companies" and "strive[s] to conduct effective advocacy for public policies that encourage the discovery of important, new medicines for patients by biopharmaceutical research companies." *See* https://phrma.org/About (accessed June 24, 2022). AstraZeneca and Takeda are members of PhRMA. *Id.*

associated with bringing a drug to market in the United States to the extent those costs are not associated with the costs of the nonclinical studies and data with which she is familiar by experience. Accordingly, I recommend that Dr. Lansita be excluded from offering any testimony as to the cost of bringing a drug to market generally.

2. Reliability

The PSC asserts that Dr. Lansita should be prevented from opining on whether Nexium or Prilosec would be approved by FDA today because such an opinion would be unreliable and speculative.[108] While she offered that opinion in her expert report, at her deposition Dr. Lansita acknowledged that she had "not reviewed any of the clinical data and can't offer an opinion" that the clinical data were sufficient.[109] Accordingly, I recommend that the motion be granted to the extent it would preclude Dr. Lansita from offering any opinion that clinical data were sufficient to justify FDA approval of Nexium or Prilosec.

This leaves the issue of whether Dr. Lansita may offer the narrower opinion she adopted at her deposition – that the nonclinical data she reviewed would be sufficient to support FDA approval today, as she "did not identify any gaps in the data package that would preclude approval."[110] Dr. Lansita's narrowed opinion is based on her review of the nonclinical materials she identified and her experience,

[108] PSC's Omnibus Mem. 48.
[109] Lansita Dep. 144:20-22.
[110] Lansita Dep. 143:1-3.

including her time at FDA reviewing nonclinical studies and in the private sector.[111] As noted above, courts have found FDA regulatory expert testimony reliable when FDA experts rely on and apply the same methods used in their work at FDA with regard to regulation of drug approval and labeling.[112] Here, the PSC has not asserted that Dr. Lansita employed a different methodology than when she worked at FDA, or even in her experience in the private sector before or after her time at FDA. I recommend that the PSC's motion be denied to the extent it seeks to preclude Dr. Lansita from opining that, based on her experience at FDA, the nonclinical data she reviewed would be sufficient to support FDA approval today.

3. Fit

The PSC does not challenge the fit of Dr. Lansita's testimony, and there is no basis in the record to question the fit of her testimony.

C. Dr. Robert Gibbons

AstraZeneca proposes to present Dr. Robert Gibbons as a general causation expert to testify on "[t]he strengths and limitations of the scientific literature concerning proton pump inhibitors (PPIs) and chronic kidney disease (CKD)" and "[w]hether the available evidence supports a causal relationship between PPIs and

[111] Lansita Expert Report 1.
[112] *See, e.g.*, *Terry II*, 2016 U.S. Dist. LEXIS 117594, at *20; *Johns*, 2021 U.S. Dist. LEXIS 143187, at *436; *Lemmon*, 2012 U.S. Dist. LEXIS 95924, at *27.

CKD."[113] The PSC seeks to exclude Dr. Gibbons's testimony on two grounds: first, that Dr. Gibbons is not qualified to provide such testimony because he is a biostatistician, not an epidemiologist, and lacks specialized nephrology training;[114] and second, that Dr. Gibbons's methodology is unscientific and unreliable because it unreasonably excludes certain data and contains erroneous calculations.[115] For the reasons set forth below, I recommend that the PSC's motion be denied.

1. Qualifications

Dr. Gibbons is a professor of biostatistics at the University of Chicago with extensive experience developing statistical methods to analyze drug safety data.[116] He has authored a book on statistics in drug safety and pharmacoepidemiology and hundreds of peer-reviewed papers.[117] He is an elected member of the National Academy of Medicine ("NAM") and the National Academy of Sciences ("NAS"), and he served for six years on the NAM Board on Health Sciences Policy.[118]

Although his principal focus in recent years has been on statistical analysis and pharmacoepidemiologic analysis with respect to psychoactive drugs, Dr.

[113] PSC's Omnibus Mem., Ex. 20 [hereinafter Amended Gibbons Expert Report] at 6, ECF No. 703-20.
[114] PSC's Omnibus Mem. 50.
[115] PSC's Omnibus Mem. 51-54.
[116] Amended Gibbons Expert Report 4-5.
[117] Amended Gibbons Expert Report 4, App. 2.
[118] Amended Gibbons Expert Report 4.

Gibbons has experience with kidney-related research.[119] He works with the NAM's Committee on Organ Transplantation on issues "focuse[d] heavily on kidney transplantation and chronic kidney disease" and performed other work involving kidney disease.[120] He also "reviewed a wide range of articles that describe the underlying background of chronic kidney disease."[121]

The PSC contends that, notwithstanding Dr. Gibbons's academic credentials and history of consulting work related to kidney disease, he lacks sufficient expertise to present his proposed statistical opinions regarding causation.[122] In particular, the PSC notes that he is a biostatistician, not an epidemiologist, and, more importantly, that he has no specialized training in nephrology or gastroenterology.[123] The PSC argues that, as a result of his lack of training in nephrology, he does not have a sufficient understanding of the meaning of the data considered to reach accurate conclusions. For example, the PSC states that Dr. Gibbons did not know that acute interstitial nephritis ("AIN") is an acute kidney injury ("AKI") and that, therefore, his treatment of AIN and AKI as independent variables skews his analysis.[124]

---

[119] AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. T [hereinafter Gibbons Dep.] at 47:17-21, 49:9-11, 51:15-22, ECF No. 734-21.
[120] Gibbons Dep. 47:6-21.
[121] Gibbons Dep. 206:10-12.
[122] PSC's Omnibus Mem. 50-51.
[123] PSC's Omnibus Mem. 50.
[124] PSC's Omnibus Mem. 50.

The PSC's criticism that Dr. Gibbons is not a formally trained nephrologist or gastroenterologist should be rejected for two reasons. First, Dr. Gibbons's practical experience with the NAM and extensive academic training and credentials in biostatistics qualify him to offer an expert opinion on questions of statistics. Biostatisticians have expertise in statistics, data analysis, and data interpretation and do not need to be experts regarding the disease pathology or treatment being analyzed.[125] Such a requirement would set an unreasonably high bar for expert epidemiological and biostatistical testimony that has no support in Third Circuit precedent.[126]

Second, the PSC's criticism is misplaced because it does not address the thrust of Dr. Gibbons's proposed testimony. His opinion evaluates the studies' methodologies and evidence of alleged causation from a statistical perspective. He considers the variables as defined in the studies, the methodological rigor of the studies, the potential role of confounding factors, and the quality of the statistical analysis of the studies. It is a statistical review and critique regarding the strength, or lack thereof, of suggested correlations as reflected in data, not an analysis of disease mechanisms and pathology. Such testimony is within his area of expertise.

---

[125] *See Hospira, Inc.*, 285 F. Supp. 3d at 811.

[126] *See, e.g.*, *Waldorf*, 142 F.3d at 626 ("[O]rdinarily an otherwise qualified witness is not disqualified merely because of a lack of academic training."); *Paoli*, 35 F.3d at 753.

To the extent that the PSC believes that Dr. Gibbons's alleged lack of knowledge regarding kidney function and disease may affect the reliability of his opinions, counsel can engage in cross-examination to challenge his credibility and address what weight the jury should give his opinions.[127]

2. Reliability

The PSC does not dispute that Dr. Gibbons used well-recognized, peer-reviewed statistical methods in developing his opinion. Rather, the PSC challenges Dr. Gibbons's application of these methods, arguing that he erroneously analyzed the Bradford Hill criteria in assessing the causal link between PPIs and adverse renal events by misapplying "temporality" criteria and purportedly "cherry-picking" data from some of the studies.[128] The PSC also argues that Dr. Gibbons erroneously grouped data in his analysis.[129] Thus, it argues, these flaws in applying his methodology render his opinion unreliable.[130]

a. Dr. Gibbons's Reliability as to His Evaluations of Other Studies

A careful review of the criticisms in the PSC's brief, Dr. Gibbons's Amended Report, and the relevant deposition testimony does not support the conclusion that Dr.

---

[127] *See U.S. v. Mitchell*, 365 F.3d at 244-45.
[128] PSC's Omnibus Mem. 51-55.
[129] PSC's Omnibus Mem. 56.
[130] *See* PSC's Omnibus Mem. 56*; In re: Zoloft*, 858 F.3d at 795 (noting that both the expert's methodology and its application must be reliable for the testimony to be admissible).

Gibbons's application of the Bradford Hill criteria is unreliable. Dr. Gibbons's analysis takes into account the potential confounding factors present in the non-randomized trial literature upon which the PSC relies, and he evaluates those studies to determine whether such confounding factors affect the reliability of those studies.[131] Dr. Gibbons's discussion of body mass index ("BMI") as a risk factor for CKD comes in the context of an in-depth review of 132 pieces of literature, not just the Lazarus, Xie, Peng, and Cho articles. Dr. Gibbons thoroughly explains his reasoning where he disagrees with the conclusions expressed by some of the authors based on their use of the data or discounts the reliability of some of the data.[132] His disagreement with the conclusions of the authors of some of the literature that he reviewed and the conclusions of the experts relied upon by the PSC does not render his analysis unreliable.

The specific examples cited by the PSC (*e,g.*, their criticism of Dr. Gibbons's discussion of the Xie study's application of the "temporality" criterion and their criticism of Dr. Gibbons' discussion of BMI as a risk factor for CKD) do not refute this conclusion.[133] As to both of these, he explains his rationale for and the methodology he used in arriving at his opinions.[134]

---

[131] *See* Amended Gibbons Expert Report 17, 30-33, 37.
[132] *See* Amended Gibbons Expert Report 18-51; AstraZeneca's Opp'n to PSC's Omnibus Mem. 39-44.
[133] PSC's Omnibus Mem. 51-52.
[134] *See* Amended Gibbons Expert Report 27-28 (Dr. Gibbons noted that FDA criticized the Xie publication on grounds similar to his); Gibbons Dep. 270:10-271:6, 282:7-287:13.

Disagreements as to the appropriate statistical evaluation of the relevant literature and the data therein are proper subjects for cross-examination at trial.[135] However, they are not sufficient to warrant exclusion under the "flexible" reliability requirement, which "is not to be used as a tool by which the court excludes all questionably reliable evidence."[136]

b. Reliability of Grouping of Data in AstraZeneca Studies

The PSC also challenges Dr. Gibbons's work as unreliable because he concededly initially improperly grouped certain AstraZeneca clinical trial data within his meta-analysis and then, after re-running his statistical models, purportedly failed adequately to modify his Report.[137]

Dr. Gibbons's initial error is not a basis for exclusion because the PSC does not dispute that it was corrected in Dr. Gibbons's Amended Report. Thus, regardless of whether the initial meta-analysis properly grouped data, the Amended Report resolves this issue. Moreover, the Amended Report was provided to the PSC prior to Dr. Gibbons's deposition, so the PSC had the opportunity to cross-examine him on the issue.[138] The PSC can cross-examine Dr. Gibbons on the issue at trial and

[135] *See Daubert*, 509 U.S. at 596.
[136] *Paoli*, 35 F.3d at 744.
[137] *See* PSC's Omnibus Mem. 56-58.
[138] *See* PSC's Omnibus Mem. 56.

can argue that the jury should consider the initial error in determining what if any weight and credibility it affords Dr. Gibbons's testimony.

More importantly, the PSC's argument that Dr. Gibbons's initial error materially affected his analysis and Amended Report does not withstand scrutiny. A comparison of the relevant charts and amended text shows that the impact was limited and that Dr. Gibbons modified his expert report to address it. The Amended Report contains a revised chart and modifies the text to state that treatment by duration interactions *were* statistically significant, as opposed to not significant in the initial draft.[139] However, it still shows (as did the initial chart) that "the estimated [glomerular filtration rate] changes from baseline are identical at 65 weeks and in fact PPI use was associated with *better* kidney function than comparators from 65 to 104 weeks."[140] Thus, while the charts look different, on their face they appear to support the same conclusion reached by Dr. Gibbons. To the extent the PSC believes that the modifications have some other significance, they can be addressed on cross-examination.

3. Fit

The PSC does not challenge the fit of Dr. Gibbons's testimony, and there is no basis in the record to question the fit of his testimony.

---

[139] *Compare* Amended Gibbons Expert Report 20-21, *with* PSC's Omnibus Mem., Ex. 15 [hereinafter Gibbons Expert Report] at 20, ECF No. 703-15.
[140] *Compare* Amended Gibbons Expert Report 20, *with* Gibbons Expert Report 20.

D. Dr. Rajat Deo

AstraZeneca seeks to offer expert testimony by Dr. Rajat Deo on the issue of specific causation – namely, that hypertension, in conjunction with other comorbidities, was a substantial contributing factor to Plaintiff Rieder's and Plaintiff Bales's CKD.[141] Specifically as to *Rieder*, AstraZeneca seeks to offer Dr. Deo's opinion that "Mr. Rieder's long-standing hypertension caused and substantially contributed to the development and progression of Mr. Rieder's CKD."[142] Similarly in *Bales*, AstraZeneca seeks to offer Dr. Deo's opinion that Plaintiff Bales's "long-standing history of hypertension, including his exaggerated stress response, and chronic [non-steroidal anti-inflammatory drug ("NSAID")] use contributed to his kidney disease[.]"[143] Additionally, in both cases, Dr. Deo's testimony is intended to rebut the testimony of Plaintiff Rieder's and Bales's specific causation expert, Dr. Morton R. Rinder, who "purports to rule out cardiovascular disease as contributing to Plaintiffs' CKD."[144]

---

[141] *See* AstraZeneca's Opp'n to PSC's Omnibus Mem. 11-13, 15-16; PSC's Omnibus Mem., Ex. 4 [hereinafter Deo Expert Report in *Bales*], ECF No. 703-4; PSC's Omnibus Mem., Ex. 5 [hereinafter Deo Expert Report in *Rieder*], ECF No. 703-5.
[142] Deo Expert Report in *Rieder* 1.
[143] Deo Expert Report in *Bales* 3.
[144] AstraZeneca's Opp'n to PSC's Omnibus Mem. 15. *See also* AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. J [hereinafter Rinder Expert Report in *Bales*] at 3, ECF No. 734-11 ("I conclude that neither hypertension nor renovascular disease were contributory factors in his development of CKD."); AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. K [hereinafter Rinder Expert Report in *Rieder*] at 3, ECF No. 734-12 ("I conclude that the etiology of Mr. Rieder's chronic kidney disease

The PSC has moved to exclude Dr. Deo's opinion testimony on two grounds: (1) that Dr. Deo is not qualified to provide a specific causation opinion as to whether Plaintiffs' PPI use caused their CKD because he is a cardiologist without specialized training in renal physiology, pharmacology, or pathology; and (2) that Dr. Deo's opinion is not reliable because he did not consider the Plaintiffs' PPI use as a potential cause of their CKD.[145] For the reasons set forth below, I recommend that the motion to exclude Dr. Deo's expert testimony be denied. However, I also recommend that, to avoid the risk of jury confusion, the Court consider giving instructions to the jury that Dr. Deo was not asked to and did not consider or form any opinion with respect to whether Plaintiff Rieder's or Plaintiff Bales's PPI use was a cause of either of their CKD.

1. Qualifications

Dr. Deo, a graduate of MIT and the University of Michigan Medical School, is trained in internal medicine and is a board-certified cardiologist and cardiac electrophysiologist. He is a clinical researcher at the University of Pennsylvania Perelman School of Medicine and his clinical practice focuses on the management of cardiac arrhythmias, especially in patients with advanced kidney disease.[146] He

---

cannot be attributed to an underlying cardiovascular disease."); Deo Dep 225:10-16; 434:22-435:5.

[145] PSC's Omnibus Mem. 23.

[146] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.

also has an NIH-funded research program that focuses on understanding the link between cardiovascular disease and CKD.[147]

The PSC argues that Dr. Deo is not qualified to give a specific causation opinion regarding the causation between PPI use and Plaintiffs' CKD: (i) because although Dr. Deo's clinical practice and academic research involve the intersection of cardiovascular disease and kidney disease, Dr. Deo is a cardiologist, not a nephrologist, and lacks specialized training in renal physiology, pharmacology, or pathology; and (ii) because Dr. Deo's focus is on cardiac disease incidental to kidney disease, he does not treat patients for CKD and, if he observes CKD in his patients, he refers those patients to nephrologists for treatment of their CKD.[148] However, Dr. Deo is not, for either plaintiff, offering an opinion that PPI use did not cause their CKD.[149] Rather, as set forth more fully below, he is opining that their hypertension and other comorbidities and conditions were substantial contributing factors to both Plaintiffs' development of CKD.

[147] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.
[148] PSC's Omnibus Mem. 25-27.
[149] AstraZeneca's Opp'n to PSC's Omnibus Mem., Ex. G [hereinafter Deo Dep.] at 354:4-6, Sep. 9, 2021, ECF No. 734-8 ("I'm not commenting one way or another on the role PPI either did or did not contribute to Mr. Rieder's CKD."); Deo Dep. 175: 11-15, Sep. 9, 2021 ("I was asked to review the Bales case especially with regards to cardiovascular disease, cardiovascular risk factors and their effect on his chronic kidney disease.").

Dr. Deo is sufficiently qualified under Third Circuit *Daubert* law. Dr. Deo is trained in internal medicine and, with board certifications in internal medicine, cardiovascular diseases and clinical cardiac electrophysiology, participates in research related to CKD, specifically the management of cardiac disease in patients with CKD.[150] Once an expert meets the baseline threshold of sufficient qualifications to proffer an expert opinion, the extent of the expert's qualifications goes to the credibility and weight to be accorded his testimony.[151] Given Dr. Deo's background, education, experience and clinical research specifically related to the intersection of cardiovascular disease and CKD,[152] he is sufficiently qualified to opine about Plaintiffs' cardiovascular issues and how they relate to Plaintiffs' CKD. Moreover, as discussed below, if Plaintiffs are permitted to present a cardiologist to opine that cardiovascular issues are not the cause of Plaintiffs' CKD, as a matter of fairness Defendants must be permitted to present a cardiologist to rebut such testimony.

2. Reliability

The PSC also asserts that Dr. Deo's testimony regarding causation fails to satisfy the reliability prong because Dr. Deo concededly did not evaluate the key causation issue in the case – whether Plaintiffs' PPI use was a cause of their CKD.[153]

---

[150] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.
[151] *Id.*
[152] Deo Expert Report in *Rieder* Ex. A; Deo Expert Report in *Bales* Ex. A.
[153] *See* PSC's Omnibus Mem. 23.

This lack of reliability is exacerbated, in the PSC's view, because Dr. Deo considered other potential causes of their CKD and attributed their CKD in part to those other conditions. Specifically, as to Plaintiff Rieder, Dr. Deo states in his report that:

> [C]onsistent with [Plaintiff Rieder's] medical history, as well as assessment of his own treating providers, it is my opinion, to a reasonable degree of medical and scientific certainty, that Mr. Rieder's CKD and renal decline is attributable to hypertension and NSAID and COX-2 inhibitor use. There are also multiple other factors throughout his records that caused or contributed to his CKD including metabolic syndrome, obesity, diabetes, and years of smoking.[154]

Similarly, with regard to Plaintiff Bales, Dr. Deo states in his report that:

> [I]t is my opinion to a reasonable degree of scientific and medical certainty that . . . hypertension and exaggerated blood pressure response with stress testing, concomitant use of NSAIDs, extensive smoking history, advanced COPD – all in combination were the substantial contributing factors to [Plaintiff Bales's] CKD. These conditions preceded development of his minor CKD, which is of far less significance to his overall prognosis than his other comorbidities such as reduced lung function/ventilatory capacity.[155]

In the PSC's view, Dr. Deo's consideration of a host of potential causative factors except Plaintiffs' PPI use renders Dr. Deo's opinion testimony unreliable and potentially misleading to the jury.[156]

The PSC's argument regarding the reliability of Dr. Deo's testimony raises an issue of the potential for jury confusion. As the Third Circuit observed in *Paoli*, "the

[154] Deo Expert Report in *Rieder* 5.
[155] Deo Expert Report in *Bales* 4.
[156] PSC's Omnibus Mem. 23-25.

core of differential diagnosis is a requirement that experts at least consider alternative causes . . . ."[157] Given that Dr. Deo addressed a variety of potential causes of Plaintiffs' CKD, Dr. Deo's omission of any discussion of Plaintiffs' PPI use, the cause alleged by plaintiffs in these cases, while not rendering his opinion completely unreliable, does bear on the credibility of his testimony.

Importantly, as previously noted, AstraZeneca has represented that it intends to call Dr. Deo specifically to rebut Dr. Rinder's opinion that cardiovascular issues were not a cause of both Plaintiffs' CKD.[158] In his expert reports, Dr. Rinder opines that Plaintiffs' CKD cannot be attributable to cardiovascular disease.[159] Like Dr. Deo, Plaintiffs' expert, Dr. Rinder, also a cardiologist, offers no opinion as to whether PPI use contributed to Plaintiffs' CKD. Dr. Deo also understood that he was being asked to consider and respond directly to Dr. Rinder's opinions[160] and he specifically did so in his reports.[161] In that context, Dr. Deo's disavowal of any

---

[157] *Paoli*, 35 F.3d at 759.
[158] *See* AstraZeneca's Opp'n to PSC's Omnibus Mem. 15-16.
[159] Rinder Expert Report in *Bales* at 3 ("I conclude that neither hypertension nor renovascular disease were contributory factors in [Plaintiff Bales's] development of CKD."); Rinder Expert Report in *Rieder* at 3 ("I conclude that the etiology of [Plaintiff] Rieder's chronic kidney disease cannot be attributed to an underlying cardiovascular disease.").
[160] Deo Depo 225:10-16; 434:22-435:5.
[161] Deo Expert Report in *Rieder* 6 ("[Dr. Rinder] improperly omits any discussion of hypertension as a cause of Mr. Rieder's CKD."); Deo Expert Report in *Bales* 4 ("I have reviewed Dr. Rinder's report…. Dr. Rinder minimizes the effects that the patient's other comorbidities such as COPD and advanced ventilatory dysfunction can have on CKD and CKD progression.").

evaluation or opinion on the impact (if any) of these Plaintiffs' PPI use on their kidney function is understandable. Given that Plaintiffs Rieder and Bales are offering their expert cardiologist, Dr. Rinder, to opine that cardiovascular disease can be ruled out as a cause of their CKD, AstraZeneca should be allowed to offer its own expert cardiologist, Dr. Deo, to opine that Dr. Rinder is incorrect and that cardiovascular disease cannot be ruled out as a cause of Plaintiffs' CKD.

3. Fit

The PSC does not challenge the fit of Dr. Deo's testimony in either *Rieder* or *Bales*, and there is no basis in the record to question the fit of his testimony in those cases.

E. Dr. Caren Palese

AstraZeneca seeks to offer Dr. Caren Palese, a gastroenterologist, as a specific causation expert to testify that Plaintiff Rieder's CKD predated his Nexium use. The PSC moved to exclude Dr. Palese's specific causation opinions as to the cause of Plaintiff Rieder's CKD. Her primary basis for this conclusion is her calculation of Plaintiff Rieder's estimated glomerular filtration rate ("eGFR")[162] in January 2002, prior to his Nexium use; she asserts that it shows abnormal kidney function at that time. The PSC challenges Dr. Palese's qualifications to give such testimony and the reliability of her testimony, given her inability to identify adequately the

[162] eGFR is calculated with a formula that accounts for blood creatinine levels and some combination of other characteristics, including age.

methodology she used to perform her calculation to arrive at her conclusion, and several misstatements made in her deposition testimony about Plaintiff Rieder's age in January 2002 (age being a data point required to calculate eGFR).[163]

For the reasons set forth below, I recommend that Dr. Palese's testimony be excluded because her conclusion that Plaintiff Rieder's CKD predated his Nexium use is not based on a defined, replicable, and reliable methodology. Admitting such testimony therefore would not "help the trier of fact to understand the evidence or to determine a fact in issue;" instead, it would create a substantial risk that the jury would be confused or misled.[164]

1. Qualifications

Dr. Palese is a board-certified gastroenterologist.[165] She completed her residency in internal medicine and was – but is not presently – board-certified in internal medicine.[166] She testified that she was "very comfortable taking care of patients with kidney disease."[167] However, she also testified that when treating patients with CKD,

[163] PSC's Omnibus Mem. 28-35.
[164] Fed. R. Evid. 702(a).
[165] PSC's Omnibus Mem., Ex. 9 [hereinafter Palese Expert Report] at 1, ECF No. 703-9.
[166] Palese Expert Report 1.
[167] PSC's Omnibus Mem., Ex. 10 [hereinafter Palese Dep.] at 145:3-4, ECF No. 703-10.

she worked on a team with nephrologists because "[u]sually you'd like to have a kidney doctor involved if the patient had chronic kidney disease."[168]

Expert testimony by physicians is very rarely excluded in the Third Circuit for lack of qualifications, and Dr. Palese satisfies the liberal Third Circuit standard for qualifications. Dr. Palese is a well-credentialed gastroenterologist with ample experience treating patients with CKD for their gastrointestinal conditions, including with PPIs.[169] She works alongside nephrologists as a member of multidisciplinary teams for her patients with CKD.[170] She reviewed over 250 documents, including peer-reviewed studies, FDA materials, and professional association guidance documents.[171] Under the Third Circuit's liberal standard, she is sufficiently qualified to provide expert testimony on the purported causal relationship between Plaintiff Rieder's PPI use and his CKD.

2. Reliability

To determine reliability, a court must look at the scientific validity of the methodology upon which the expert bases an opinion.[172] As set forth above, an

[168] Palese Dep. 143:21-23.
[169] Palese Dep. 71:3-72:5, 75:14-76:2.
[170] *See, e.g.*, Palese Dep. 143:2-23.
[171] Palese Expert Report Ex. B. Dr. Palese's qualifications considerably exceed those of the doctor who was excluded as unqualified in *Diaz v. Johnson Matthey, Inc.*, 893 F. Supp. 358, 372 (D.N.J. 1995), because he had never treated a patient with the particular respiratory condition at issue, was unfamiliar with the literature on the condition, and lacked any other qualifications beyond his general training and credentials.
[172] *Paoli*, 35 F.3d at 742.

expert must identify the methodology or procedures used to explain how the expert's conclusions were reached, and the data and materials considered by the expert must be available.

The relevant facts do not appear to be in dispute. Dr. Palese does not routinely calculate eGFR for her patients in her practice as a gastroenterologist.[173] To support her opinion that Plaintiff Rieder suffered from CKD in January 2002, prior to his Nexium use, Dr. Palese went on the internet and found a formula that she says that she used to calculate Plaintiff Rieder's eGFR using his creatinine levels, age, and gender.[174] Dr. Palese did not keep any record of that calculation or of the inputs she used and could not identify with certainty at her deposition the formula she used.[175] She erroneously stated throughout her deposition that Plaintiff Rieder was in his thirties in January 2002, when he was actually forty-four at that time.[176] Though she corrected this error in later deposition testimony after being shown a document that

[173] Palese Dep. 187:12-19.
[174] Palese Dep. 187:20-188:4; Oral Args. 178:10-15, Apr. 4, 2022.
[175] Palese Dep. 189:3-21. Defense counsel at oral argument agreed that Dr. Palese could not identify the formula she had used: "And Ms. Martines is right, [Dr. Palese] cannot remember the website … to which she inputted, but what she says is that … combining her experience and with the calculations that she did, it results in an eGFR of 60." Oral Args. 178:10-15, Apr. 4, 2022. In other words, Dr. Palese could not recall where she got the formula that she used, but nonetheless concluded that 60 was the correct number – even though at her deposition she misstated one of the key inputs (age) multiple times and admitted that she did not make this calculation routinely in her practice.
[176] *See, e.g.*, Palese Dep. 158:17-22, 161:16-22, 162:5-24.

contained his date of birth, there is no record in her report of the age she used in her eGFR calculation.[177] The only potential evidence that she used the correct age is her *ipse dixit* assertion at deposition that she did use the correct age, after being corrected about repeatedly misstating Plaintiff Rieder's age in her deposition testimony.[178]

AstraZeneca asserts that calculating eGFR is just like converting Fahrenheit to Celsius, so it does not matter that Dr. Palese cannot show her work. My review of the available internet eGFR calculators reveals that they are not all identical, so it is possible that the specific calculator used would affect the result.[179] Because Dr. Palese kept no records of her calculation and does not know where she got the

[177] Palese Dep. 162:15-163:16.
[178] Palese Dep. 172:13-21.
[179] A review of eGFR calculators available on the internet shows that there is variability as to inputs. The National Kidney Foundation one uses: serum creatinine (mg/dL); serum cystatin C (mg/L); age (years); gender (m/f); standard assays (y/n/not sure); adjust for body surface (y/n/not sure). Nat'l Kidney Foundation, *eGFR Calculator*, https://www.kidney.org/professionals/kdoqi/gfr_calculator (last visited June 24, 2022). A "Medline Plus" calculator from the National Library of Medicine uses creatinine, age, weight, height, gender, and race. MedlinePlus, *Glomerular Filtration Rate (GFR) Test*, https://medlineplus.gov/lab-tests/glomerular-filtration-rate-gfr-test/ (last visited June 24, 2022). A calculator from DaVita Kidney Care uses serum creatinine, age, and gender. DaVita Kidney Care, *GFR Calculator*, https://www.davita.com/tools/gfr-calculator (last visited June 24, 2022). One available on "Calculator.net" uses serum creatinine (mg/dL), age, gender, race (black/not black). Calculator.net, *GFR Calculator*, https://www.calculator.net/gfr-calculator.html (last visited June 24, 2022).

calculator on the internet, she has not identified a methodology that can be evaluated by the Court or that can be repeated by Dr. Palese or others.[180]

Courts in this Circuit presented with similar circumstances have rejected expert opinions as unreliable. In *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Practices & Prods. Litig.*, the court noted that where the data the expert used in his analysis were permanently unavailable and the analysis could not possibly be repeated, the methodology was unreliable.[181] Similarly, in *Buzzerd*, an expert's testimony was ruled inadmissible when he failed to articulate any methodology used to develop his opinion and relied solely on his observations and *ipse dixit* conclusions.[182]

The same is true here. Dr. Palese's methodology consists of searching online for an eGFR formula, choosing one, and using it to calculate Plaintiff Rieder's eGFR without recording which formula she chose, the source of the formula, the data she inputted, or consideration of the availability of alternative methodologies. Dr. Palese's calculation of Plaintiff Rieder's eGFR cannot be reproduced because it is

[180] The PSC's counsel noted in oral argument that she had attempted to replicate Dr. Palese's analysis and result using a calculator that Dr. Palese had indicated was one that she might have used but was unable to replicate Dr. Palese's calculated result. Oral Args. 174:15-19, Apr. 4, 2022.

[181] *In re Johnson & Johnson Talcum Powder*, 509 F. Supp. 3d at 155.

[182] *See Buzzerd*, 669 F. Supp. 2d at 523; *U.S. v. Mitchell*, 365 F.3d at 235 (noting other factors that may be relevant include "whether a method consists of a testable hypothesis" (quoting *Paoli*, 35 F.3d at 742 n.8)).

unknown what calculator she used or what inputs she put into it, and she cannot demonstrate how this calculation generated the result she claims to have gotten.

3. Fit

The PSC does not challenge the fit of Dr. Palese's testimony, and there is no basis in the record to question the fit of her testimony.

IV. DEFENDANTS' MOTIONS

A. Dr. David Ross

The PSC seeks to offer expert testimony by Dr. David Ross on FDA's process for approving drug labeling, requiring and evaluating post-marketing safety and efficacy data, considering label modifications, and the adequacy of the warnings provided by AstraZeneca for Nexium and Takeda for Prevacid (in *Bales*) regarding a possible causal association between these drugs and renal impairment. AstraZeneca seeks to exclude Dr. Ross's opinion testimony for lack of qualifications, reliability, and fit.[183] Additionally, AstraZeneca seeks to exclude his potential testimony relating to the FDA's level of understanding of the difference between acute tubulointerstitial nephritis ("ATIN") and chronic tubulointerstitial nephritis ("CTIN") and the adequacy of FDA staffing and resources.[184] Takeda

[183] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Ross 1-2 [hereinafter AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross], No. 2:19-cv-00850, ECF No. 33-1; *Daubert*, 509 U.S. at 589-92.

[184] AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 1-2.

moves to exclude Dr. Ross's opinion on the grounds of reliability and fit, as well as additional arguments that Dr. Ross may not, as a matter of law, opine that the warnings were inadequate at the time of Prevacid approval and that his opinions about Takeda's pharmacovigilance improperly constitute a "fraud on the FDA" claim.[185] For the reasons discussed below, I recommend that these motions be denied in substantial part. With regard to two narrow arguments made by AstraZeneca, as discussed in more detail below, I recommend that the motion be granted.

1. Qualifications

Dr. Ross has multiple degrees and post-doctoral training relevant to the issues in these cases. He received both an M.D. and a Ph.D. in Biochemistry from New York University and a master's degree in Biometrics from Oregon Health Sciences University.[186] He completed a residency in internal medicine at New York University ("NYU") and a fellowship in infectious disease at Yale University School of Medicine.[187]

Prior to joining FDA in 1996, Dr. Ross was a practicing physician focusing on HIV/AIDS patients from 1991-1996. From 1996-2006, Dr. Ross held multiple

[185] Mem. in Supp. of Takeda's Mot. to Exclude Test. of Dr. David Ross 14 [hereinafter Takeda's Mem. in Supp. of Mot. to Exclude Ross], No. 2:17-cv-06124, ECF No. 77-1.
[186] AstraZeneca's Mot. to Exclude Ross, Ex. A [hereinafter Ross Expert Report] at Ex. A, 1, No. 19-cv-00850, ECF No. 33-3.
[187] Ross Expert Report Ex. A, 1.

positions at FDA: Medical Officer at the Division of Anti-Infective Drug Products, Senior Medical Reviewer at the Division of Anti-Infective Drug Products, Medical Team Leader at the Division of Anti-Infective Drug Products, Deputy Director at the Office of Drug Evaluation VI, and Associate Director for Regulatory Science at the Office of Oncology Drug Products.[188] His work at FDA involved reviewing and making approval recommendations for INDs and NDAs, reviewing labeling changes (including Changes Being Effected ("CBEs")), providing guidance on post-marketing surveillance of adverse events, reviewing reports submitted to FDA by NDA sponsors, and ultimately supervising and directing more junior medical reviewers at FDA.

Dr. Ross was repeatedly recognized for professional excellence at FDA: for example, he received the CDER Excellence in Communication Award (ODE IV/PhRMA Working Group), the CDER Team Excellence Award (Maxipime® Review Team), the CDER Group Recognition Award (Inter-Divisional Working Group on Antibiotic Resistance), the FDA Commendable Service Award (Linezolid Review Team), the FDA Award of Merit (CDER Counter-Terrorism Response Team), and the CDER Team Excellence Award (CDER TOPOFF 2 Exercise Team).[189]

Since 2006, Dr. Ross has been the Director of HIV, Hepatitis, and Related Conditions Programs in the Office of Specialty Care Services at the Veteran's Health

[188] Ross Expert Report 2-3.
[189] Ross Expert Report Ex. A, 3-4.

Administration and has also served as a staff physician at the VA Medical Center in Washington, DC. He is board-certified in internal medicine and infectious diseases and has an extensive list of publications and presentations, most relating to infectious disease issues and some relating to drug development and study design.[190]

AstraZeneca does not challenge Dr. Ross's qualifications generally, but only as to the following: (1) his opinions regarding whether PRAC properly analyzed data submitted by AstraZeneca; and (2) his opinions regarding pharmacology, toxicology, and nephrology, particularly as applied to preclinical and clinical trials.

Dr. Ross is trained in internal medicine and has over a decade of experience at FDA reviewing preclinical and clinical trial data, adverse event data, and product labeling relating to a variety of medical specialties. The fact that he is not holding himself out as an expert in nephrology, for example, does not mean that he is incapable of providing expert opinions about the adequacy and interpretation of preclinical or clinical trial data or subsequent analyses of those data simply because he is not an expert in that particular substantive field.[191] FDA reviewers have expertise in reviewing, interpreting, and analyzing data and that is what he is proposing to do here. Likewise, the fact that he did not ever work for PRAC does

[190] Ross Expert Report 3-17.

[191] Indeed, AstraZeneca has argued that Dr. Lansita, an expert in toxicology, is qualified to offer an expert opinion on the regulatory significance of animal studies she reviewed despite the fact that she is not an expert in nephrology.

not preclude him from opining about the adequacy of PRAC's data analysis.[192] Here, Dr. Ross is being proffered to testify about data analysis from a regulatory perspective. Dr. Ross is highly qualified under applicable Third Circuit law to testify about this subject matter given his decade-long experience doing just that at FDA.[193]

2. Reliability

AstraZeneca and Takeda both argue that Dr. Ross's testimony fails to satisfy *Daubert*'s reliability prong because Dr. Ross fails to provide adequate explanations for how he reached his conclusions about an association between Nexium use and ATIN and CTIN.[194]

Dr. Ross provided a 275-page report in which he described the voluminous materials that he reviewed as well as the approach that he took in reviewing these materials and reaching his conclusions.[195] He explained the regulatory process

---

[192] As the PSC's brief notes, Dr. Ross's criticisms focus largely on analyses of the data that he believes that AstraZeneca, not PRAC, should have performed. PSC's Mem. in Supp. of its Opp'n to AstraZeneca's Mot. to Exclude Dr. David Ross 37-38, ECF No. 737 [hereinafter PSC's Opp'n Mem. to AstraZeneca's Mot. to Exclude Ross].

[193] *See Terry I*, 2016 U.S. Dist. LEXIS 99177, at *14-15 (finding that an expert with eighteen years of experience who contributed to the labeling and promotional materials of more than one hundred different products was qualified to conduct research in the same way FDA would); *Wolfe I*, 881 F. Supp. 2d at 658 (finding FDA experts to be qualified to testify regarding a drug's regulatory compliance even when their work done at FDA did not include review of draft labeling and they only received general "regulatory science" training).

[194] *See* AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 7-10; Takeda's Mem. in Supp. of Mot. to Exclude Ross 7-12.

[195] Ross Expert Report 14-16, Ex. C.

governing pharmaceuticals, including the process for obtaining initial approval, how and when a manufacturer may seek to modify label warnings and the applicable regulations, and FDA's historical practice in considering such applications.[196] He described his methodology based on his education, training, and experience at FDA applying the applicable FDA regulations.[197] While Defendants may disagree with his analysis, it cannot fairly be said that his methodology is not systematic and explained.

An expert's methodology is reliable if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.[198] As noted above, courts have found the experience at FDA to be particularly valuable for FDA experts testifying on regulatory issues, especially when coupled with additional industry or academic experience.

The cases relied upon by Defendants are distinguishable and reflect extreme situations not presented here. In *In re Trasylol Prods. Liab. Litig.*, Dr. Suzanne Parisian's report suffered from several fatal flaws not present in this case.[199] First, unlike in this case, there was a substantial question whether Dr. Parisian, whose FDA experience related to medical devices, was qualified to testify regarding FDA

[196] Ross Expert Report 19-73.
[197] *See* Ross Expert Report 15-16.
[198] *See* Fed. R. Evid. 702; *Paoli*, 35 F.3d at 741.
[199] *In re Trasylol Prods. Liab. Litig.*, 709 F. Supp. 2d 1323 (S.D. Fla. 2010).

regulatory processes involving pharmaceuticals, which are subject to different regulations and handled by a separate division.[200] Second, in *Trasylol*, Dr. Parisian's conclusion required a causal opinion that she could not give.[201] Third, Dr. Parisian "conducted only a cursory and conclusory look at Trasylol from the perspective of the plaintiffs in this case" and included problematic opinions based exclusively on speculation concerning FDA's and Bayer's intent, including statements that Bayer continued to expand the Trasylol sales force when they were aware that FDA changed its risk-benefit profile and assumptions about FDA's concerns regarding the warnings.[202] Fourth, as Defendants correctly noted, the court in *Trasylol* found that Dr. Parisian generally took a collection of facts, speculated to impute motive, and drew unsupported conclusions unrelated to her regulatory expertise.[203] Dr. Ross's report is far different from Dr. Parisian's report. Rather, Dr. Ross's report is an in-depth review and analysis of voluminous records, data, peer-reviewed literature and data analysis of the type he regularly reviewed at FDA and from which he draws supported conclusions related to his regulatory expertise that he adequately explains. Finally, unlike in this case, *Trasylol* involved a witness whom the court

[200] *Id.* at 1331.
[201] *Id.*
[202] *Id.* at 1338.
[203] *See id.* at 1348; AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 9.

found to be evasive and not credible when questioned and who had been repeatedly rejected as an expert or criticized by other courts.[204]

*In re TMI Litiga*tion is similarly distinguishable in that the expert Dr. Vladimir Shevchenko's methodology was open to attack due to his admission that he relied on "his own ipse dixit, rather than on something more verifiable" and that his methodology changed in response to challenges.[205]

It is clear that Dr. Ross, with a decade of experience reviewing INDs, NDAs, labeling proposals, and adverse drug event data and recommending

---

[204] *See, e.g.*, *Trasylol*, 709 F. Supp. 2d at 1345 n.29 ("In the past, courts have had trouble limiting Dr. Parisian's testimony, despite her and the plaintiffs[']assurance, that she would not exceed its proper scope. . . . Dr. Parisian also demonstrated at the *Daubert* hearing that she was unable or unwilling to connect her opinions to any valuable regulatory expert analysis and opined on matters that were far beyond her expertise." (citation omitted)); *see also Rowland v. Novartis Pharms. Corp.*, 9 F. Supp. 3d 553 (W.D. Pa. 2014) (excluding Dr. Parisian's causation testimony); *Bartoli v. Novartis Pharms. Corp.*, No. 3:13-0724, 2014 U.S. Dist. LEXIS 52956 (M.D. Pa. Apr. 17, 2014) (limiting Dr. Parisian's regulatory testimony and excluding all her other proposed testimony); *In re Human Tissue Prods. Liab. Litig.*, 582 F. Supp. 2d 644 (D.N.J. 2008) (finding Dr. Parisian's reliability particularly troubling and granting the motion to exclude); *In re Prempro Prods. Liab. Litig.*, 554 F. Supp. 2d 871, 879-87 (E.D Ark. 2008) (noting that Dr. Parisian's testimony should not have been permitted); *Lopez v. I-Flow Inc.*, No. CV 08-1063, 2011 WL 1897548 at *11 (D. Ariz, Jan. 26, 2011) (finding that Dr. Parisian's testimony lacked reliability and helpfulness to the jury); *Hines v. Wyeth*, No. 2:04-0690, 2011 WL 2680842 at *5 (S.D. W.Va, July 8, 2011) (finding that Dr. Parisian's testimony was "neither relevant nor reliable under *Daubert* and Rule 702"); *In re Fosamax Prods. Liab. Litig.*, 645 F. Supp. 2d 164, 192 (S.D. N.Y. 2009) (limited Dr. Parisian's commentary to explaining the regulatory context in which they were created and stating that she was not permitted to read, quote from, or regurgitate her reports).

[205] *In re TMI Litig.*, 193 F.3d at 687-88.

regulatory action based on his review, is employing a reliable methodology to do the same in these cases.

3. Fit

Defendants argue that Dr. Ross's testimony concerning the potential association between PPIs and ATIN and CTIN should be excluded because it is not a fit with the issues presented in these six Bellwether Trial Cases. Their argument is that because all six plaintiffs claim to have developed CKD, there is no fit between (1) Dr. Ross's proposed testimony regarding the information available to AstraZeneca and Takeda about the association between PPI use and development of ATIN and CTIN and his conclusion that the labeling at various points in time was inadequate and (2) the injuries claimed by the plaintiffs in the six Bellwether Trial Cases.

In making this argument, Defendants ignore the scientific/medical relationship between ATIN/CTIN and CKD, oversimplify and misstate the failure to warn claims made by these plaintiffs, and take isolated testimony given by Dr. Ross about CKD entirely out of context.

The crux of Defendants' lack of fit argument is that the PSC is alleging that AstraZeneca and Takeda failed to warn specifically of an association between PPI use and CKD and that Dr. Ross's testimony pertains to whether and when AstraZeneca and Takeda had sufficient information about an association between

PPI use and development of ATIN or CTIN. This argument misses the point. The PSC argues that AstraZeneca and Takeda were on notice as early as 1995 of an association between ATIN and PPI use, and by 2003 of an association between CTIN and PPI use, and that they should have provided adequate warnings of these associations because, among other things, these conditions can lead to CKD.[206]

Dr. Ross's report likewise makes it clear that ATIN or CTIN are relevant to this litigation because if these conditions develop and are undetected and/or left untreated, they can lead to CKD.[207] Dr. Ross's report contains a lengthy and detailed review of scientific publications, clinical trial data, and post-marketing adverse event data linking PPI use with ATIN and CTIN.[208] Based upon these data, he concluded, "The connection between acute and chronic injury in the tubulointerstitium is grounded in the understanding that interstitial nephritis constitutes "a final common pathway to all forms of end-stage renal disease.'"[209]

He further concludes that the risk that PPI use could have an adverse effect on the kidneys was known to AstraZeneca and Takeda by the late 1990's and that "the

---

[206] PSC's Mem. in Supp. of its Opp'n to Takeda's Mot. to Exclude Test. of Dr. David Ross 5-6, ECF No. 745 ("PPI use is known to cause a kidney injury known as interstitial nephritis ("IN"), now called tubulointerstitial nephritis ("TIN"). It has been recognized for decades that TIN can manifest as acute tubulointerstitial nephritis ("ATIN") or chronic tubulointerstitial nephritis ("CTIN") and that both of these entities separately can lead to [CKD] and End Stage Renal Disease ("ESRD").")

[207] Ross Expert Report 94-98.

[208] Ross Expert Report 98-248.

[209] Ross Expert Report 270.

threshold of reasonable evidence of a causal association between PPI use and chronic, progressive renal toxicity was crossed by early 2003."[210] Failure to warn of this risk, in Dr. Ross's view, resulted in the lack of monitoring and treatment of PPI users so that the renal injury would go undetected until it had progressed to CKD.[211]

With this context, Defendants' reliance on two quotes from Dr. Ross do not support Defendants' argument of lack of fit. AstraZeneca asserts that "Dr. Ross testified unequivocally during his deposition that the conditions with which he was concerned, ATIN and CTIN, are different ailments from CKD."[212] Of course Dr. Ross made this distinction, because ATIN and CTIN are in fact different from CKD. However, this argument ignores Dr. Ross's views that are discussed above about the relevance of ATIN and CTIN to this litigation – that left untreated, they can and do lead to CKD. Similarly, Defendants cite the statement in Dr. Ross's report that "[i]n 2016, Lazarus *et al*, was the first group of scientists to report on the association between PPI and CKD" for the proposition that there could be no failure to warn claim prior to 2016.[213] Again, that is not an accurate characterization of Dr. Ross's opinions, which link ATIN and CTIN to potential development of CKD.

[210] Ross Expert Report 271-272.
[211] Ross Expert Report 272-274.
[212] AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross 5.
[213] Ross Expert Report 133.

Defendants will of course present experts who disagree with Dr. Ross's conclusions and will cross-examine him vigorously, and the jury will need to decide who is right on this critical issue. However, there is no question that Dr. Ross's proposed testimony bears directly on key issues in this litigation.

4. Additional Arguments

a. AstraZeneca

AstraZeneca makes two additional arguments for excluding portions of Dr. Ross's testimony. First, it argues that any testimony relating to FDA's understanding of the difference between ATIN and CTIN should be excluded. In Dr. Ross's deposition, AstraZeneca's counsel asked him whether he thought FDA understood the difference and he responded that he did not.[214] I do not understand that the PSC intends to offer affirmative testimony by Dr. Ross regarding FDA's understanding of the difference between ATIN and CTIN. Further, it is not entirely clear to me why AstraZeneca chose to elicit this testimony at his deposition. In any event, it would be speculative and should not be offered at trial, and to that extent, I recommend granting AstraZeneca's motion.[215] However, if on cross-examination at trial AstraZeneca

[214] AstraZeneca's Mem. in Supp. of Mot. to Exclude Ross, Ex. B [hereinafter Ross Dep.] at 318:19-319:1, No. 2:17-cv-06124, ECF No. 33-3 ("Q. You think FDA understands the difference between acute ATIN and chronic TIN for purposes of labeling? . . . The Witness: All I can say is they do not. They say acute or chronic so . . . .").

[215] *Paoli*, 35 F.3d at 742.

seeks to use Dr. Ross's deposition testimony, or again to elicit testimony from Dr. Ross that he believes FDA did not understand the difference between ATIN and CTIN, for purposes of impeachment or otherwise, then AstraZeneca will have opened the door to such testimony and it should be permitted.[216]

Second, AstraZeneca seeks to exclude any testimony about FDA's staffing and resources. To the extent Dr. Ross is relying both upon his personal experience at FDA and upon objective evidence of such issues, including FDA staffing and enforcement data, at or around the period when he contends newly acquired information warranted additional PPI label warnings (*e.g.*, the 2007 Institute of Medicine report),[217] he should be permitted to testify as to that evidence.[218] However, I recommend that AstraZeneca's motion be granted to exclude any speculative testimony about FDA's resources in 2020 and their impact on the agency's ability to negotiate labeling changes at that time.[219] Dr. Ross's tenure at FDA ended in 2006 so that his personal experience is not likely to be relevant to the staffing and resources of the agency fourteen years later.

---

[216] *Healy v. Haverford Twp.*, 462 Fed. Appx. 224 (3d Cir. 2012) **(**"The doctrine of 'opening the door,' sometimes referred to as 'curative admissibility,' provides that when one party introduces inadmissible evidence, the opposing party thereafter may introduce inadmissible evidence to rebut or explain the prior evidence." (citing *Gov't of V.I. v. Archibald*, 987 F.2d 180, 187 (3d Cir. 1993)).

[217] Ross Expert Report 48 n.36.

[218] *See, e.g.*, Ross Expert Report 12-14.

[219] *See* Fed. R. Evid. 611.

b. Takeda

Takeda likewise makes two additional arguments for excluding portions of Dr. Ross's testimony, both of which should be rejected. First, it argues that Dr. Ross's testimony concerning the language that he believes should have been in the labeling "by 1995" is an impermissible attack on the initial FDA-approved Prevacid labeling and thus, by law, must be excluded. In support of this argument, it cites one First Circuit case, *Celexa*, which found that a plaintiff's claim about the inadequacy of the initial labeling was preempted.[220] Takeda then cites cases excluding testimony that was found to be contrary to established law.[221] The *Celexa* holding, however, is far from established law. For example, *Gaetano v. Gilead Scis., Inc.*, a decision from the District of New Jersey that found that there was no law preventing Gilead from implementing stronger warning language prior to approval so there was no preemption, was not even cited by Takeda.[222] Further, one of the cases cited by Takeda, *Stube v. Pfizer*,[223] directly contradicts the *Celexa* holding, finding that defendants could have submitted stronger warning language prior to the approval of the drug, and thus there

[220] Takeda's Mem. in Supp. of Mot. to Exclude Ross 13 (citing *In re Celexa and Lexapro Marketing and Sales Prac. Litig.*, 779 F.3d 34 (1st Cir. 2015)).
[221] Takeda's Mem. in Supp. of Mot. to Exclude Ross 13-14 (citing *Terry II*, 2016 U.S. Dist. LEXIS 117594; *In re Gadolinium-based Contrast Agents Prods. Liab. Litig.*, No. 1:08-GD-50000, 2010 U.S. Dist. LEXIS 43444 (N.D. Ohio May 4, 2010)).
[222] *Gaetano v. Gilead Scis., Inc.*, 529 F. Supp. 3d 333, 345 (D.N.J. 2021).
[223] 446 F. Supp. 3d 424, 435-36 (W.D. Ark. 2020).

was no preemption.[224] That appears to be exactly Dr. Ross's opinion here, and there is no legal basis to argue that such testimony should be excluded.

Second, Takeda also makes a cursory argument that Dr. Ross's testimony about Takeda's conduct regarding their regulatory obligations somehow constitutes a fraud on the FDA claim. They provide no legal support for this proposition, and, as the PSC points out, there is case law finding that former FDA officials relying on their training and experience at FDA may testify as to the appropriateness of a company's regulatory conduct.[225]

B. Dr. Martin Wells

The PSC has proffered the testimony of Dr. Martin Wells, a biostatistician at the University of Chicago, to analyze Defendants' 2016 submissions to PRAC regarding the safety of their PPI products.[226] Dr. Wells performed meta-analyses of data submitted by AstraZeneca and Takeda to PRAC in 2016 and opines that his analyses show a statistically significant decrease in renal function, as measured by eGFR, in PPI

[224] *See* Takeda's Mot. to Exclude Ross 13-14 (citing *Stube v. Pfizer, Inc.*, 446 F. Supp. 3d 424, 435-36 (W.D. Ark. 2020)).
[225] PSC's Mem. in Supp. of its Opp'n to Takeda's Mot. to Exclude Test. of Dr. David Ross 43 (citing *In re Mirena IUD Prods. Liab. Litig.*, 169 F. Supp. 3d 396, 480 (S.D.N.Y. 2016); *Kruszka v. Novartis Pharms. Corp.*, 28 F. Supp. 3d 920, 931 (D. Minn. 2014)).
[226] PSC's Mem. in Opp'n to Defs.' Mot. to Exclude Op. Test. from Dr. Martin T. Wells 5, ECF No. 739 [hereinafter PSC's Opp'n Mem. to Wells].

users as compared to non-users.[227] AstraZeneca and Takeda challenge Dr. Wells's opinions as unreliable claiming that he (1) first performed an analysis of AstraZeneca's data including their four-week studies and then, because he was unhappy with the result, excluded those four-week studies from his analysis so as to get his desired result, and (2) lacked a valid basis for including data from the eight-week AstraZeneca study in his analyses of AstraZeneca's data.[228] Defendants also argue that his opinion does not fit the issues in these cases.[229] The PSC subsequently stipulated that it does not oppose the Defendants' motions to the extent they seek to prevent Dr. Wells from offering an opinion on general causation that PPIs cause CKD or an opinion that Dr. Wells's analyses establish that PPIs are harmful to the kidneys.[230]

For the reasons set forth below, I recommend that the Court grant the Defendants' motions to the extent that they prohibit Dr. Wells from offering an opinion that PPIs cause CKD or an opinion that his analyses establish that PPIs are harmful to the kidneys, per the PSC's stipulation, but recommend denying the

---

[227] Mem. in Supp. of AstraZeneca's Mot. to Exclude Expert Test. of Dr. Martin Wells, Ex. D at 9-10 [hereinafter Wells Expert Report] No. 2:17-cv-00850, ECF No. 34-5.
[228] *See* AstraZeneca's Mem. of Law in Supp. of Defs.' Mot. to Exclude Expert Test. of Dr. Martin Wells 9-11, No. 2:17-cv-00850, ECF No. 34-1 [hereinafter Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells]; AstraZeneca and Takeda's Joint Mem. in Supp. of Defs.' Mot. to Exclude Expert Test. of Dr. Martin Wells 9-11, No. 2:17-cv-06124, ECF No. 76-1 [hereinafter Defs.' Joint Mem. to Exclude Wells].
[229] *See* Mem. in Supp. of Defs.' Mot. to Exclude Wells 4; Defs.' Joint Mem. to Exclude Wells 4.
[230] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 11.

Defendants' motions to exclude Dr. Wells' testimony to the extent that evidence regarding PRAC or its conclusions is offered into evidence at trial in any of the six Bellwether Trial Cases.[231]

1. Qualifications

Defendants do not challenge Dr. Wells's qualifications, and there is no basis in the record to question his qualifications to offer his stated opinions.

2. Reliability

AstraZeneca and Takeda assert that Dr. Wells's opinions are unreliable because he found a statistically significant decrease in eGFR in PPI users only after allegedly "cherry-picking" the data by excluding the results of studies involving only four weeks of use.[232]

---

[231] At oral argument, in response to my question whether AstraZeneca would be offering PRAC data at trial, AstraZeneca's counsel stated that "AstraZeneca intends to move to exclude foreign regulatory [submissions]" and one should "not assume that [AstraZeneca] will be relying on PRAC at trial." Oral Args. 15:15-20, Apr. 4, 2022. In the *Rieder* case, while AstraZeneca moved to exclude evidence of PPI labels approved by foreign regulatory agencies, neither party moved to exclude all evidence of data submitted to PRAC. AstraZeneca's Mot. *In Limine* to Exclude Evid. of Foreign PPI Labels, No. 2:19-cv-00850, No. ECF 60.

[232] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 12; Mem. in Supp. of Defs.' Mot. to Exclude Wells 12. Defendants also criticize Dr. Wells for not including an analysis of all 22 AstraZeneca trials in his expert report. However, AstraZeneca's counsel received the data files from plaintiffs' counsel and questioned Dr. Wells about the files at his deposition. *See* AstraZeneca's Mot. to Exclude Wells, Ex. B [hereinafter Wells Dep.] at 46:10-48:4, No. 2:19-cv-00850, ECF No. 34-4; *see also Reed v. Binder*, 165 F.R.D. 424, 429 (D.N.J. Mar. 27, 1996) ("The test of a[n expert] report is whether it was sufficiently complete, detailed and in compliance with the [Federal Rules of Civil Procedure] so that surprise is eliminated, unnecessary

Dr. Wells's testimony is unclear as to precisely when he decided to exclude AstraZeneca's four-week studies from his analysis of AstraZeneca's data. Dr. Wells testified that his decision to exclude the four-week studies was not made after he completed an initial analysis of the AstraZeneca data; rather, he did so "early on" when he read a comment by a PRAC member that highlighted the potential issues with studies shorter than twelve weeks and when he became aware that Takeda, in contrast to AstraZeneca, had submitted only those studies to PRAC that were longer than three months, consistent with the PRAC member's comment.[233] Dr. Wells testified that that he "wanted to follow the same rules across . . . the two analyses. And so that's when [he] made the decision" to exclude the data from the four-week studies from his analysis of AstraZeneca data.[234] Other parts of Dr. Wells's testimony are a bit murkier as to

---

depositions are avoided, and costs are reduced."). As set forth in more detail herein, Defendants, however, have not demonstrated that Dr. Wells decided to exclude the four-week studies after performing an initial analysis of AstraZeneca's data.

[233] Wells Dep. 83:1-21. European Meds. Ass'n, Signal Assessment Report 11 ("The limitation in duration [of renal function adverse events in clinical trials ≥ 12 weeks duration] is based on the Kidney Disease Outcomes Quality Initiative (KDOQI) definition of CKD."). At the time of Takeda's submissions to PRAC, KDOQI defined CKD as the presence of kidney damage and/or decreased GFR for three or more months. *Compare* Nat'l Kidney Foundation, Kidney Disease Outcomes Quality Initiative, Clinical Practice Guidelines For Chronic Kidney Disease: Evaluation, Classification and Stratification 44-59 (2002), https://www.kidney.org/sites/default/files/docs/ckd_evaluation_classification_stratification.pdf (EMA definition), *with* Kidney Disease Improving Global Outcomes, KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease 5 (2012), https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf.

[234] Wells Dep. 83:13-21.

exactly when he made the decision to exclude the four-week studies.[235] However, Defendants have not identified any testimony that he actually performed any statistical analysis of the AstraZeneca data before he decided to exclude the four-week studies.

Dr. Wells has provided other explanations for his decision to exclude four-week studies: the comment by the PRAC member;[236] his discussions with Dr. Lafayette and Dr. Powers, whom Dr. Wells understood to say that they would not expect to see elevated eGFR in four weeks;[237] his review of literature;[238] and the results of his heterogeneity analysis of the data of the four-week studies.[239] Thus, even if he decided to exclude the four-week studies after he performed an initial analysis of all 22 studies from AstraZeneca's PRAC data, Dr. Wells has adequately explained his reasons for doing so.

---

[235] Dr. Wells testified that one of the reasons he did not need to do a subgroup analysis before excluding the four-week studies from the AstraZeneca data from his analysis was because had spoken to two nephrologists retained by plaintiffs' counsel in this litigation, Dr. Richard Lafayette and Dr. David Powers, and they told Dr. Wells that the four-week studies would not show an effect. Wells Dep. 142:9-143:3. At another point, Dr. Wells testified that he could not remember whether he had performed any statistical analysis prior to speaking to them in around February or March 2021. Wells Dep. 145:14-24. At another point, Dr. Wells testified that it was his intent to exclude the four-week studies from his analysis of AstraZeneca's data before he performed any of his statistical analyses because he "wanted to have a balance between what Takeda did and what AstraZeneca did." Wells Dep. 83:22-84:10.

[236] Wells Dep. 83:13-21.

[237] Wells Dep. 170:24-172:12.

[238] Wells Dep. 145:19-146:3, 147:4-7.

[239] AstraZeneca's Mot. to Exclude Wells, Ex. C [hereinafter Wells Expert Report] at 6-7, App. A at Figures 1-2, No. 2:19-cv-00850, ECF No. 34-5.

Defendants also argue that Dr. Wells's analyses are internally inconsistent – and thus unreliable – because he included an eight-week study in his analysis of the AstraZeneca data but only used twelve-week studies in his analysis of the Takeda data. They point to the decisions in the *Byetta* litigation for the proposition that such disparate treatment is arbitrary and undercuts the reliability of his opinion.[240] However, this is not the apples-to-apples comparison the Defendants suggest – there were no Takeda studies under twelve-weeks submitted to PRAC. Viewing Dr. Wells's decision as to include all studies greater than four-weeks in his analyses, he has treated the AstraZeneca and Takeda data the same. It is simply because there are no Takeda studies under twelve weeks that were submitted to PRAC that there are none included in his analyses of Takeda's data.

To the extent Defendants are arguing that Dr. Wells's inclusion of the eight-week AstraZeneca study data undercuts reliability because it is inconsistent with one of his grounds for exclusion of the AstraZeneca four-week study data, the argument is unpersuasive.[241] As explained above, while Dr. Wells did note that one of his grounds for excluding four-week study data was that Takeda had not submitted data

[240] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 8; Mem. in Supp. of Defs.' Mot. to Exclude Wells 8; *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3d 1007, 1038 (S.D. Cal. 2021); *In re Byetta Cases*, No. JCCP4574, 2021 WL 2462800, at *5-6 (Cal. Super. Ct. Apr. 6, 2021.

[241] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 10-11; Mem. in Supp. of Defs.' Mot. to Exclude Wells 10-11.

from studies less than twelve weeks' duration, his testimony also reflected other grounds for excluding studies of four weeks' duration. To the extent Defendants seek to challenge Dr. Wells on his decisions, it is a matter for cross-examination as to the explanations he has provided, not a basis for exclusion.[242]

AstraZeneca and Takeda cite out-of-circuit federal and state court decisions in litigation involving the drug Byetta, in which Dr. Wells's testimony was excluded as unreliable.[243] The facts in those cases are distinguishable. In those cases, unlike here, Dr. Wells could not explain why it made sense to exclude data from one randomized clinical trial ("RCT") but not another, and it was the plaintiffs' counsel who decided which data to exclude from his analysis.[244] Unlike in this case, in *Byetta*, Dr. Wells erroneously excluded a study from his meta-analysis based on a misunderstanding of the facts about that study and did not correct that error when he learned of the correct facts.[245]

---

[242] *Daubert*, 509 U.S. at 596; *see also Heller*, 167 F.3d at 152.
[243] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 8 (citing *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3d at 1037-40; *In re Byetta Cases*, 2021 WL 2462800, at *5-6); Mem. in Supp. of Defs.' Mot. to Exclude Wells 8 (citing same).
[244] *See In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3 at 1038; *In re Byetta Cases*, 2021 WL 2462800, at *5-6.
[245] *See In re Byetta Cases*, 2021 WL 2462800, at *6; *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. at 1038.

Defendants' final challenge to the reliability of Dr. Wells's testimony is that he used summary statistics instead of patient-level data.[246] While Defendants argue that patient-level data of all of the AstraZeneca studies would change his results, they do not argue that patient-level data of the same studies Dr. Wells actually used, excluding the four-week studies, would change the results of the analyses that Dr. Wells performed. Further, Defendants do not dispute that the summary-level data that Dr. Wells analyzed were data that they themselves provided to PRAC and fail to explain why relying on those summary-level data, even if they were not the best data, should result in exclusion of his testimony. Rather, these points are ones that Defendants can make on cross-examination.

3. Fit

AstraZeneca and Takeda also challenge Dr. Wells's testimony on the grounds that it does not fit the case because it pertains only to their PRAC submissions, which they may choose not to introduce at trial.[247] While AstraZeneca's counsel indicated at oral argument that one cannot assume AstraZeneca will introduce PRAC data at trial, neither Plaintiff Rieder nor AstraZeneca sought to exclude or limit evidence of PRAC in their motions *in*

[246] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 11; Mem. in Supp. of Defs.' Mot. to Exclude Wells 11.
[247] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Wells 4-7; Defs.' Joint Mem. to Exclude Wells 4-7.

limine. Takeda's counsel indicated at oral argument that Takeda does not plan to introduce PRAC data at trial.[248]

At this time, it is unclear whether evidence of data provided to PRAC or PRAC's analysis or conclusions will be introduced into evidence at trial in any of the six Bellwether Trial Cases. To the extent such evidence is admissible, Dr. Wells's analysis satisfies the fit prong.

C. Dr. David Charytan

The PSC seeks to offer an opinion on general causation from Dr. David Charytan that the use of PPIs increases the risk of adverse renal outcomes, including development of CKD. AstraZeneca has moved to exclude Dr. Charytan, claiming that his testimony is unreliable because he purportedly used a conclusion-oriented methodology for evaluating medical literature and studies and he was purportedly inconsistent and biased in the weight that he gave to the study findings that support his opinion.[249] For the reasons set forth below, I recommend that AstraZeneca's motion to exclude Dr. Charytan's general causation testimony be denied.

1. Qualifications

AstraZeneca does not challenge Dr. Charytan's qualifications, and there is no basis in the record to question his qualifications to offer his stated opinions.

[248] Oral Args. 16:3-7, Apr. 4, 2022.
[249] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 17-23, No. 2:19-cv-00850, ECF No. 37-1.

2. Reliability

a. Use of Bradford Hill Criteria

Dr. Charytan's testimony is based upon a significant body of medical literature that he opines supports a causal relationship between PPIs and CKD. He reviewed observational studies, including Lazarus *et al.* (2016) and Xie *et al.* (2016), and meta-analyses of observational studies, as well as individual case reports and case series.[250] He concluded that "the observational studies, in the aggregate" demonstrate a causal relationship between PPI use and kidney disease.[251] In forming his opinion, Dr. Charytan relied on the Bradford Hill criteria, nine metrics commonly used by epidemiologists to distinguish a causal connection from a mere association.[252]

AstraZeneca does not dispute that the Bradford Hill criteria are a well-recognized methodology for assessing causation that can satisfy the *Daubert* reliability standard.[253] However, AstraZeneca relies on the Third Circuit's statement

---

[250] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. BB [hereinafter Charytan Expert Report] at 19-22, No. 2:19-cv-00850, ECF No. 37-30.

[251] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. C at 201:3-13 [hereinafter Charytan Dep.] No. 2:19-cv-00850, ECF No. 37-5.

[252] *See* Charytan Expert Report 34-37; *see, e.g.*, *In re: Zoloft*, 858 F.3d at 795 (citing and explaining Bradford Hill criteria).

[253] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 15-16; *In re: Zoloft*, 858 F.3d at 796; *Glynn v. Merck Sharp & Dohme Corp. (In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.)*, No. 11-5304, 2013 U.S. Dist. LEXIS 51552, at *10 (D.N.J. Apr. 10, 2013).

that "[t]o ensure that the Bradford Hill/weight of the evidence criteria 'is truly a methodology, rather than a mere conclusion-oriented selection process . . . there must be a scientific method of weighting that is used and explained.'"[254] AstraZeneca argues that Dr. Charytan's assessment of study findings using the Bradford Hill criteria was "arbitrary" and that the methodology he applied to evaluate and weigh these study findings was a "conclusion-oriented selection process" as opposed to "scientific method."[255]

The Third Circuit has held that if an expert applies a recognized methodology unevenly "without explanation, this raises an inference of unreliable application of methodology."[256] Accordingly, in assessing reliability, it is necessary to address the Dr. Charytan's application of the Bradford Hill criteria and his explanations for any apparent inconsistencies.

b. Application of Bradford Hill Criteria

Dr. Charytan explained at considerable length his application of the Bradford Hill criteria and his underlying reasoning in affording varying degrees of weight to the numerous studies he reviewed.[257] His expert report and deposition testimony

[254] *In re: Zoloft*, 858 F.3d at 796 (citing *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 607 (D.N.J. 2002)).
[255] *See In re: Zoloft*, 858 F.3d at 796.
[256] *Id.* at 797.
[257] Three pages of his expert report and a significant portion of his deposition testimony discuss each of the nine Bradford Hill criteria in relation to the medical literature he reviewed. *See* Charytan Expert Report 34-37; Charytan Dep. 187:11-215:23.

discuss the numerous randomized controlled trials ("RCTs"), observational studies, reports, and case series that he reviewed before offering his opinion that there is an increased risk of CKD when using PPIs.[258] Dr. Charytan's report and testimony also reflect that he identified and discussed the comparative strengths and weaknesses of different types of studies (*e.g.*, RCTs vs. observational studies),[259] as well as design and other limitations that affect the reliability of those studies in detecting potential causal relationships.[260]

Thus, to the extent Dr. Charytan does not give all of the literature equal weight, that decision is not "without explanation" and therefore does not, on its face, undermine the reliability of his application of the Bradford Hill criteria.[261] As a general matter, criticisms of an expert's explanations for reliance on, or rejection of, particular studies, are appropriately addressed through cross-examination, not through wholesale exclusion of the expert testimony.[262] That is the appropriate course here.

---

[258] Charytan Expert Report 16-24.
[259] Charytan Dep. 190:5-191:25, 260:7-266:17, 272:4-8, 302:1-304:1.
[260] *See* Charytan Expert Report 19-24; Charytan Dep. 192:9-194:19, 303:22-318:6.
[261] *See In re: Zolo*ft, 858 F.3d at 797.
[262] *See Hoffeditz*, 2017 U.S. Dist. LEXIS 123493, at *13-14. In its reply brief, AstraZeneca cites *Loeffel Steel Prods., Inc. v. Delta Brands, Inc.*, 387 F. Supp. 2d 794, 800 (N.D. Ill. 2005), but that out-of-circuit case is factually distinguishable. *See* Reply Mem. in Further Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 3, No. 2:19-cv-00850, ECF No. 55. There, unlike here, the court excluded the testimony as unreliable because the expert used a unique, idiosyncratic definition of an economic term that was not peer-reviewed or generally accepted in the profession and relied on defendant-provided information the validity of which he was "incapable of assessing." *Loeffel Steel Prods., Inc.*, 387 F. Supp. 2d at 803-07.

AstraZeneca's other specific criticisms do not demonstrate that Dr. Charytan's methodology was so arbitrary and unreliable as to require exclusion under Rule 702 and *Daubert*.

First, AstraZeneca criticizes Dr. Charytan for not applying a specific evaluation tool when assessing "the potential for bias in each of the observational studies on which he relies."[263] In particular, AstraZeneca argues that Dr. Charytan's disagreement with a conclusion in an FDA Department of Epidemiology review that the Lazarus *et al.* (2016) and Xie *et al.* (2016) studies suffered from design flaws which precluded finding a causation link between the use of PPIs and developing CKD is unreliable because he did not use "any formal tool to assess it."[264] However, AstraZeneca cites no law requiring the use of a "formal tool." Dr. Charytan explained his reasoning: he testified that he believed FDA's findings were too conservative and failed to look at some evidence and science that he would have considered.[265] The issue implicated here – "evaluation of possible biases or confounding factors found in the studies" – is properly addressed through cross-examination, rather than exclusion.[266]

---

[263] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 22.
[264] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 23.
[265] Charytan Dep. 292:2-294:12.
[266] *See* PSC's Mem. in Opp'n to AstraZeneca's Mot. to Exclude Pls.' General Causation 9, ECF No. 743; *Fosamax* 2013 U.S. Dist. LEXIS 51552, at *10-11 (allowing a general

Second, AstraZeneca asserts that Dr. Charytan's criticism of the reliability of the Moayyedi *et al.* 2019 study because of, among other things, its reliance on telephone interviews, while simultaneously relying on the Lazarus study, which also used telephone interviews, is inconsistent and arbitrary.[267] Dr. Charytan testified, however, that it is not the telephone interview technique itself that can result in bias, but the purpose and execution of the telephone interviews,[268] which he evaluated when determining how to assess the risk of bias.[269] He explained that the Moayyedi study failed to explain sufficiently how investigators obtained information during their phone calls.[270] Dr. Charytan also noted additional grounds for questioning the reliability of the Moayyedi study.[271] Dr. Charytan has provided an explanation for

---

causation expert to testify when the expert's methodology was sufficiently reliable and explicitly noting that any issues could be addressed on cross-examination).

[267] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 19.

[268] Charytan Dep. 306:8-13, 307:7-9. Dr. Charytan admitted the bias introduced by the use of the telephone to obtain information would be present in RCT and observational studies and explains, "you have to get into the weeds and figure out exactly what questions they asked, when they were asking it, how, what information they were seeking, but…it's not specific to the telephone interview per se, or the use of telephone…I think it depends on the questions asked…and the information being looked for."

[269] Charytan Dep. 305:8-308:2.

[270] *See* Charytan Dep.306:8-308:13; Charytan Expert Report 23.

[271] These additional grounds included that the PPI portion of the study was designed to detect gastrointestinal bleeding prevention as opposed to CKD; creatinine levels, which are a common indicator of kidney function, were only tested during initial screening instead of with routine checks; and over 22% of the participants already had CKD at the start of the study. Charytan Expert Report 22-23.

the purported inconsistencies that AstraZeneca can probe and challenge on cross-examination.

Third, AstraZeneca criticizes Dr. Charytan's conclusion that the three-year follow up period in Moayyedi "may have been too short to detect most cases of CKD."[272] Dr. Charytan identified several reasons why a longer reporting period may be preferential, including under-reporting or delayed reporting of symptoms when interviewed during studies or questioned by doctors in less-obvious cases.[273] Again, AstraZeneca can challenge Dr. Charytan's explanation on cross-examination.

Finally, AstraZeneca argues that Dr. Charytan should have given more weight than he did to the Attwood article, which did not identify CKD as a serious adverse event associated with PPI use.[274] The Attwood article summarizes certain safety data obtained from two AstraZeneca trials, titled SOPRAN and LOTUS, where researchers studied the effects of PPIs omeprazole and esomeprazole, respectively.[275] Dr. Charytan provided several reasons why he does not believe the

---

[272] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 19; Charytan Dep. 306:14-307:9, 308:3-8.
[273] *See* Charytan Dep. 169:7-172:10.
[274] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 20.
[275] Stephen E. Attwood *et al.*, *Long-term safety of proton pump inhibitor therapy assessed under controlled, randomized clinical trial conditions: data from the SOPRAN and LOTUS studies*, 41 Alimentary Pharmacology & Therapeutics 1162, 1162 (2015).

findings of the two trials disprove his opinion that PPI use can cause CKD.[276] The trials were designed to evaluate the effectiveness of PPIs, rather than renal safety. There was no detailed description of the data on kidney function reported. The mean age of participants was young, and the trials excluded people with "significant comorbidities, suggesting that they enrolled populations at low risk of kidney disease."[277] The sample sizes for the two trials were small, 154 and 266 participants, respectively.[278] In short, Dr. Charytan provided an explanation for why the fact that CKD was not identified as a serious adverse event associated with PPI use during either the SOPRAN or LOTUS trials did not necessarily mean that PPI use is not a risk factor for development of renal disease.[279] Again, AstraZeneca can cross-examine him as to whatever flaws it sees in that explanation.[280]

3. Fit

AstraZeneca does not challenge the fit of Dr. Charytan's testimony, and there is no basis in the record to question the fit of his testimony.

---

[276] Charytan Expert Report 23.
[277] Charytan Expert Report 23.
[278] Charytan Expert Report 23.
[279] Charytan Expert Report 23.
[280] Dr. Charytan explained that CKD "would rarely be reported as a [serious adverse event ("SAE")] because it's generally not going to be considered as an SAE unless you're specifically looking for it in the trial and defining it as such" and that "this would be an issue where trying to assess the occurrence of CKD in a clinical trial on the basis of SAE reports would likely lead to marked under-counting of the events." Charytan Dep. 313:6-9, 314:13-16.

D. Dr. Wajahat Mehal

The PSC proffered Dr. Wajahat Mehal, a gastroenterologist and professor at the Yale School of Medicine, to testify regarding general causation, the adequacy of Nexium labeling, and issues regarding marketing and purported overprescribing of PPIs. AstraZeneca moved to exclude all of Dr. Mehal's testimony, arguing that he is not qualified to testify regarding marketing and the adequacy of labeling, his testimony regarding general causation is unreliable, and his testimony regarding an objective test for diagnosing gastroesophageal reflux disease ("GERD") is irrelevant and does not fit the case.[281] The PSC subsequently agreed that it does not oppose AstraZeneca's motion to the extent it seeks to prevent Dr. Mehal from testifying "on the adequacy of the label in a regulatory context."[282]

For the reasons set forth below, I recommend that the motion to exclude Dr. Mehal be granted to the extent it seeks to prevent Dr. Mehal from testifying about the adequacy of the labeling in the regulatory context, per the stipulation from the PSC, medical marketing generally, and the impact of medical marketing on sales, but otherwise denied. However, this would not prevent Dr. Mehal from testifying about the "Montreal definition" in cases where specific testing for GERD did not occur.

[281] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35.
[282] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 10.

1. Qualifications

AstraZeneca argues that Dr. Mehal is not qualified to offer an expert opinion on the adequacy of labeling or on the role of medical marketing and its impact on the prescribing of PPI products.[283]

Dr. Mehal earned his medical degree from the University of Oxford in England in 1989 and subsequently completed his residency in internal medicine and fellowship in gastroenterology at the Yale School of Medicine.[284] He has been on the faculty at Yale since 2001.[285] He has been board-certified in internal medicine since 1997 and obtained a sub-certification in gastroenterology in 2001.[286] He is currently a tenured Professor of Medicine, a practicing clinician specializing in digestive diseases and gastroenterology, and a researcher in the areas of gastrointestinal disease and tissue injury and repair.[287]

At his deposition, Dr. Mehal testified that he is not a regulatory expert "so [he] won't be speaking about regulatory issues such as label warnings

---

[283] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 39-40.
[284] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. A [hereinafter Mehal Expert Report] at 4-5, No. 2:19-cv-00850, ECF No. 37-3.
[285] Mehal Expert Report 5.
[286] Mehal Expert Report 5.
[287] Mehal Expert Report 5.

specifically."[288] Dr. Mehal and the PSC also stipulated at his deposition that Dr. Mehal will not be offering an opinion about the adequacy of the 2020 labeling.[289] Subsequently, the PSC stipulated that it does not oppose AstraZeneca's motion to the extent it seeks to prevent Dr. Mehal from testifying "on the adequacy of the label in a regulatory context."[290] Thus, there is no dispute that Dr. Mehal cannot testify about the adequacy of the labeling.

Dr. Mehal proposes to opine regarding medical marketing of PPIs and its impact. In his report he cites articles noting the increase in spending on medical marketing across all medications, including PPIs, from 1997 to 2016.[291] He also opines on some concerns regarding medical marketing by citing to articles regarding the economic impact of coupons and rebates and selective information, and notes that marketing strategies include disease awareness campaigns prior to launching a product. He states that changes in medical marketing over the past 20 years have had "direct bearing on the high use of PPIs" and that the large numbers of patients exposed to PPIs worldwide are "attributable in great part to medical marketing efforts of the defendant manufacturers."[292]

---

[288] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts, Ex. B [hereinafter Mehal Dep.] at 360:12-14, No. 2:19-cv-00850, ECF No. 37-4.
[289] Mehal Dep. 357:2-22.
[290] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 10.
[291] Mehal Expert Report 48-49.
[292] Mehal Expert Report 48, 50.

The PSC asserts that Dr. Mehal's opinions regarding medical marketing are based on the marketing he has seen and his clinical judgment as a gastroenterologist and prescriber of PPIs and is supported by peer-reviewed medical literature.[293] However, Dr. Mehal does not identify any marketing he has seen as a clinician or in preparing his testimony, and his citations to information about medical marketing spending overall and general criticisms about medical marketing generally do not provide a basis to link unidentified marketing of unidentified drugs to an increase in PPI use. The PSC does not suggest that Dr. Mehal has any formal training on medical marketing or its impact on sales of PPIs or any particular product. I credit Dr. Mehal's own testimony on the matter when he testified that he is *not* an expert on regulatory labeling or medical marketing issues.[294]

2. Reliability

As with Dr. Charytan, AstraZeneca does not dispute that Dr. Mehal's general causation opinion is based on a review and lengthy discussion of the abundant literature on PPIs, including RCTs, observational studies, reports, case series, and meta-analyses and consideration of the Bradford-Hill factors.[295] And, as with Dr. Charytan, AstraZeneca argues that Dr. Mehal's opinion is not reliable because it

[293] PSC's Mem. in Opp'n to AstraZeneca's Mot. to Exclude Pls.' General Causation 102-04.
[294] Mehal Dep. 80:10-81:21.
[295] *See* Mehal Expert Report 23-47, 52-63; Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 17-24, 33-35.

disagrees with his conclusions regarding the methodological strength and reliability of the various studies and his conclusion that the RCTs are not conclusive on the issue of causation.[296] AstraZeneca argues that Dr. Mehal's analysis was result-driven and he "failed to base his opinion on 'sufficient facts and data' or reliably apply 'principles and methods to the facts of the case' to satisfy Rule 702 standards of admissibility.[297]

In particular, AstraZeneca does not agree with Dr. Mehal's analysis in which he does not deem as dispositive the results of two RCTs, the Moayyedi and Attwood studies, which he determined to be flawed.[298] Dr. Mehal explained that he did not give the Moayyedi and Attwood studies conclusive weight because they "were not specifically designed to investigate whether PPIs cause CKD."[299] His explanation and other discussion in his report are sufficient to satisfy the Third Circuit's *Daubert* reliability standards.[300]

AstraZeneca also asserts that Dr. Mehal "cherry-picked" and did not use a consistent methodology because he did not reject observational studies on which he relied that, like the RCTs, "were not specifically designed" to investigate whether

---

[296] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35.
[297] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35.
[298] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 33-35; Mehal Expert Report 30-32.
[299] Mehal Expert Report 31-32.
[300] *See Heller*, 167 F.3d at 152; *In re TMI Litig.*, 193 F.3d at 665; *Paoli*, 35 F.3d at 744-46; *Hoffeditz*, 2017 U.S. Dist. LEXIS 123493, at *13-14.

PPIs cause CKD.[301] AstraZeneca maintains that this disparate treatment indicates that he did not reliably weigh all the evidence, but instead gave more weight to studies that support his desired conclusion.[302] However, this ignores the extensive explanation in Dr. Mehal's report and deposition of the multiple factors that informed his determination regarding what weight he assigned to a study's findings, including the scale, design, power, and manner of collecting data.[303]

The reliability requirement does not mandate a particular type of study, and AstraZeneca does not cite to any authority that would prohibit an expert from looking beyond RCTs to other types of studies to assess general causation.[304] Here, Dr. Mehal has explained his reasoning for not giving conclusive weight to the RCTs and giving greater weight to other studies. AstraZeneca can cross-examine Dr.

---

[301] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 34.

[302] Reply Mem. in Further Supp. of AstraZeneca's Mot. to Exclude General Causation Experts 33, No. 2:19-cv-00850, ECF No. 55.

[303] *See* Mehal Expert Report 23-47, 52-63; *see also* Mehal Expert Report 25 ("[E]ach of the described lines of evidence have both strengths and weaknesses, but they complement each other. Thus, if the findings are consistent across multiple studies of varying types, even if not perfectly correlated, they provide a very high level of conviction that a cause-and-effect relationship has been established. In addition to examining the types of studies which are providing evidence, it is important to examine the tempo of the findings. Were there a few early studies based on incomplete data, which could not be reproduced, or has the evidence been building up year after year as more data is collected? In my opinion, the latter is true regarding PPI-induced nephrotoxicity of PPIs."); Mehal Dep. 244:7-24, 417:24-418:7.

[304] *See*, *e.g.*, *Heller*, 167 F.3d at 154-55 (declining to require a physician to rely on definitive published studies to make a diagnosis because the physician reliably used a different generally accepted methodology).

Mehal to challenge his reasoning, but I believe that the proposed testimony satisfies the Third Circuit's reliability requirement.

AstraZeneca relies on *Hollander v. Sandoz Pharms. Corp.*[305] to argue that Dr. Mehal's opinion is unreliable because it relies on observational studies which it claims cannot, standing alone, establish causation.[306] But that out-of-circuit case is distinguishable. Unlike in this case, where Dr. Mehal relies on numerous epidemiological studies and meta-analyses, the experts in *Hollander* did not rely on epidemiological studies.[307] And, unlike in *Hollander*, Dr. Mehal is not relying on evidence that the court has determined is unreliable.[308]

AstraZeneca also seeks to exclude Dr. Mehal's proposed testimony that the majority of patients who stop using PPIs resume taking them due to exacerbation of their symptoms because Dr. Mehal based his opinion on studies in healthy patients, not patients with GERD.[309] However, the record reflects that Dr. Mehal based his opinion on studies, multiple peer-reviewed publications, and meta-analyses,[310] as well as his own experience as a practicing gastroenterologist who prescribes PPIs

---

[305] 289 F.3d 1193 (10th Cir. 2002).
[306] *See* Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 34.
[307] *Hollander*, 289 F.3d at 1211.
[308] *Id.* at 1208.
[309] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' General Causation Experts 38.
[310] Mehal Expert Report 15.

for GERD.[311] He testified that in order to determine "whether PPIs can result in rebound, you need to do it in healthy patients, because these are people who don't have GERD. If you do this study in GERD patients…and they get symptoms, it's difficult to know if it's rebound to PPIs or if it's just recurrence of their prior disease."[312] Given Dr. Mehal's experience and the literature upon which he relies, I do not find AstraZeneca's argument persuasive. AstraZeneca can challenge Dr. Mehal on cross-examination on these issues at trial.

3. Fit

Plaintiffs' claims include that "[d]efendants made statements, affirmations and representations of fact concerning their PPI products through their advertisements, educational campaigns and multi-platform marketing and promotional initiatives directed at consumers, patients and healthcare providers promoting unnecessary and dangerous use and overuse of their PPI products."[313] Dr. Mehal opines that the broadened, functional definition of GERD developed at a meeting in Montreal in 2006 (the "Montreal definition") and included in a publication funded by AstraZeneca led to an increase in GERD diagnoses and subsequent "overuse" of PPIs. AstraZeneca argues that Dr. Mehal's testimony on this issue should be excluded because it does not fit the issues in this case.

---

[311] Mehal Dep. 40:4-19.
[312] Mehal Dep. 169:6-13.
[313] Pls.' Master Long Form Compl. and Jury Demand ¶ 381, ECF No. 118.

It is undisputed that PPIs are used to treat GERD. It is also undisputed that plaintiffs' claims include the assertion that multiple defendants overpromoted PPIs through various methods, including educational campaigns. However, not every case involves the allegation that a particular plaintiff was put on PPIs as a result of the Montreal definition. If in any case there is evidence that the individual plaintiff was placed on PPIs as a result of the application of the Montreal definition of GERD, rather than testing specifically confirming GERD, Dr. Mehal's testimony on the issue, as applied to that individual plaintiff, would satisfy the fit standard. Otherwise, I recommend that his proposed testimony on this issue should be excluded.

E. Dr. Derek Fine

The PSC has proffered Dr. Derek Fine, a nephrologist at Johns Hopkins Hospital, as a specific causation expert to testify that Plaintiff Rieder's use of Nexium was a cause of his CKD, as well as the progression of his kidney disease.[314] Dr. Fine has also offered opinions on general causation in a separate report from his opinions on Plaintiff Rieder,[315] but AstraZeneca has not moved to exclude Dr. Fine's

[314] AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts, Ex. X [hereinafter Fine Specific Causation Expert Report] at 8-12, No. 2:19-cv-00850, ECF No. 35-26.

[315] PSC's Br. Opposing Defs.' Mots. for Summ. J. on Failure to Warn Preemption, Ex. 329 [hereinafter Fine General Causation Expert Report], ECF No. 731-83.

general causation opinions.[316] AstraZeneca asserts that Dr. Fine's specific causation testimony as to Plaintiff Rieder should be excluded as unreliable because Dr. Fine purportedly fails to explain why hypertension and obesity are not the only causes of Plaintiff Rieder's CKD and because there is not a sufficient evidentiary basis for Dr. Fine's conclusion that Nexium substantially contributed to Plaintiff Rieder's CKD.[317] For the reasons set forth below, I recommend that AstraZeneca's motion to exclude Dr. Fine's specific causation testimony as to Plaintiff Rieder be denied**.**

1. Qualifications

AstraZeneca does not challenge Dr. Fine's qualifications, and there is no basis in the record to question his qualifications to offer his stated opinions.

2. Reliability

AstraZeneca, relying on *Heller*, argues that Dr. Fine does not reliably explain why hypertension and obesity are not the only causes of Plaintiff Rieder's CKD.[318] In *Heller*, the Third Circuit, citing *Paoli*, stated that "where a defendant points to a plausible alternative cause and the doctor offers *no* explanation for

[316] At oral argument, AstraZeneca's counsel acknowledged that AstraZeneca is not challenging Dr. Fine's testimony on general causation. Oral Args. 118:2-3, Apr. 4, 2022 ("[W]e are not challenging Dr. Fine's general causation report here[.]").
[317] Mem. Of Law in Supp. of AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts 26-27, No. 2:19-cv-00850, ECF No. 35-1 [hereinafter AstraZeneca's Specific Causation Mem.].
[318] AstraZeneca's Specific Causation Mem. 28.

why he or she has concluded that was not the sole cause, that doctor's methodology is unreliable."[319]

Dr. Fine does not dispute that hypertension, when poorly controlled, can cause CKD, but disagrees that hypertension was the sole cause of Plaintiff Rieder's CKD.[320] Dr. Fine testified that Plaintiff Rieder's hypertension was generally well controlled with medication so that his blood pressure was not severely elevated in most of the available readings, with the exception of one time in 2003.[321] As further evidence that hypertension was not the sole cause of Plaintiff Rieder's CKD, Dr. Fine pointed to times when Plaintiff Rieder's GFR was declining even when his blood pressure was well controlled.[322] Dr. Fine explained "there were times when [Plaintiff Rieder's blood pressure] was beautifully controlled, and GFR was still overall declining. So I don't think there is enough evidence to say that hypertension was a substantial contributor."[323]

AstraZeneca challenges Dr. Fine's explanation by noting that the goal for CKD patients is to keep systolic blood pressure at less than 130 mmHg and that Plaintiff Rieder's systolic blood pressure was at or above 130 mmHg on forty-six of the ninety

---

[319] *Heller*, 167 F.3d at 156.
[320] AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts, Ex. Y [hereinafter Fine Dep.] at 71:16-72:3, 160:1-8, No. 2:19-cv-00850, ECF No. 35-27.
[321] Fine Dep. 322:6-10.
[322] Fine Dep. 303:11-305:17.
[323] Fine Dep. 322:11-15.

dates.[324] But AstraZeneca did not question Dr. Fine at his deposition as to the significance, if any, of Plaintiff Rieder's occasionally but not consistently high systolic blood pressure readings or how elevated his systolic blood pressures would need to have been, how consistently, and for how long, in order for Dr. Fine to have considered hypertension to have caused Plaintiff Rieder's CKD. Overall, the record does not support a claim that Dr. Fine has provided no reasoned, scientifically based explanation for his exclusion of hypertension as a sole cause of Plaintiff Rieder's CKD. AstraZeneca can cross-examine Dr. Fine on these points at trial, but it has not shown that his testimony on this issue is so unreliable as warrant exclusion under *Daubert*.

The same is true as to obesity. Dr. Fine acknowledges that obesity has been associated with the development of CKD, although he observes that the actual role of obesity in the etiology of CKD is controversial.[325] Dr. Fine observed that Plaintiff Rieder was only mildly, not extremely, obese.[326] Dr. Fine further opined that the changes in Plaintiff Rieder's creatinine levels (which can indicate kidney disease) over time were inconsistent with kidney disease in a person with his actual level of

[324] Reply Mem. in Further Supp. of AstraZeneca's Mot. to Exclude Specific Causation Experts 31-32, No. 2:19-cv-00850, ECF No. 54.
[325] Fine Specific Causation Expert Report 11 (opining that "[i]t is more likely that obesity instead associates with diabetes and hypertension such that any association of obesity with renal injury is driven by obesity's impact on these two health conditions." (internal citation omitted)).
[326] Fine Dep. 275:2-6.

obesity.[327] AstraZeneca disputes Dr. Fine's conclusions as to the role of obesity in his CKD, arguing that Plaintiff Rieder's BMI was over twenty-five for an extended period of time and that his proteinuria levels decreased when he lost weight.[328] These points are appropriately the subject of cross-examination, but do not support exclusion of Dr. Fine's testimony.

3. Fit

AstraZeneca does not challenge the fit of Dr. Fine's testimony, and there is no basis in the record to question the fit of his testimony.

F. Dr. Gilbert Moeckel

The PSC has proffered the testimony of Dr. Gilbert Moeckel on the animal studies performed by PPI manufacturers, including AstraZeneca and Takeda, as part of the drug approval process. AstraZeneca has moved both to disqualify Dr. Gilbert Moeckel from testifying[329] and to exclude his testimony, contesting his qualifications to opine on animal pathology and the reliability and fit of his testimony.[330] Takeda has also moved to exclude Dr. Moeckel from testifying on the

[327] Fine Dep. 303:19-305:17.
[328] Reply Mem. in Supp. of AstraZeneca's Mot. to Exclude Pls.' Specific Causation Experts 32-33, No. 2:19-cv-00850, ECF No. 54.
[329] Mem. of Law in Supp. of AstraZeneca's Mot. to Disqualify Dr. Moeckel, No. 2:19-cv-00850, ECF No. 36-1 [hereinafter AstraZeneca's Mem. to Disqualify Moeckel].
[330] Mem. of Law in Supp. of AstraZeneca's Mot. to Exclude Dr. Moeckel 1, No. 2:19-cv-00850, ECF No. 35-1 [hereinafter AstraZeneca's Mem. to Exclude Moeckel].

same grounds of qualification, reliability, and fit.[331] The PSC stipulated that it does not oppose the Defendants' motions to the extent that they seek to prevent Dr. Moeckel from offering an opinion that PPIs cause acute or chronic kidney disease in humans or from using animal evidence to prove general causation.[332]

For the reasons set forth below, I recommend that AstraZeneca's motion to disqualify Dr. Moeckel be denied. I recommend that the Defendants' motions to preclude Dr. Moeckel from offering an opinion that PPIs cause acute and chronic kidney disease in humans or from using animal evidence to prove general causation be granted, per the PSC's stipulation, but they be denied as to the rest of Dr. Moeckel's opinions. To the extent that Defendants have raised issues about whether Dr. Moeckel's testimony and opinions are credible and well-supported by the data that he reviewed, they can address such issues through cross-examination of Dr. Moeckel at trial.

1. Motion to Disqualify Dr. Moeckel

AstraZeneca contends that Dr. Moeckel "surreptitiously switched sides" by becoming an expert for plaintiffs after meeting once with counsel for AstraZeneca, leading AstraZeneca to "operate[] under a reasonable assumption that the parties entered a confidential consulting relationship for nearly four years."[333] In

[331] Mem. of Law in Supp. of Takeda's Mot. to Exclude Dr. Moeckel 1-2, No. 2:17-cv-06124, ECF No. 80 [hereinafter Takeda's Mem. to Exclude Moeckel].
[332] Joint Report to the Special Master Re *Daubert* Mot. Oral Args. ¶ 12.
[333] Mem. of Law in Supp. of AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel 1, No. 2:19-cv-00850, ECF No. 36-1.

opposition, the PSC argues that while Dr. Moeckel met with AstraZeneca's counsel once and subsequently received notebooks with medical literature from them, he was never retained by them nor did he receive any payment from them or learn any confidential information from them.[334] For the reasons set forth below, I recommend that AstraZeneca's Motion to Disqualify Dr. Moeckel be denied.

The record reflects the following facts relevant to AstraZeneca's motion to disqualify: On November 14, 2016, counsel for AstraZeneca from the law firm Ice Miller LLP telephoned Dr. Moeckel and then sent a confirmatory e-mail stating "[t]hank you for your time today to speak with Katherine regarding consulting with us in the Nexium/kidney litigation. At your convenience, would you please forward us your retainer agreement via return e-mail."[335] Two days later, counsel at Ice Miller sent another e-mail reiterating their interest in working with Dr. Moeckel and requesting a CV.[336] In response, Dr. Moeckel provided a fee schedule and a one-page document titled "CONSULTING AGREEMENT BETWEEN DR. GILBERT MOECKEL AND ICEMILLER LEGAL COUNSEL" that was signed by Dr.

[334] *See* AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. E, [hereinafter Declaration of Katherine Althoff] No. 2:19-cv-00850, ECF No. 36-7; Oral Args. 43:1-44:1, Apr. 4, 2022.
[335] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. A [Hawkins E-mail, Nov. 14 & 16, 2016] No. 2:19-cv-00850, ECF No. 36-3.
[336] Hawkins E-mail, Nov. 14 & 16, 2016.

Moeckel.[337] This so-called "Consulting Agreement" contained Dr. Moeckel's fee terms but did not contain any provisions regarding the scope of work or confidentiality. Ice Miller never signed that "Consulting Agreement," nor did it ever provide Dr. Moeckel with any retainer agreement of its own.[338]

Dr. Moeckel met with AstraZeneca's counsel on January 16, 2017, for two hours. AstraZeneca asserts that it shared confidential information with Dr. Moeckel at that meeting and would not have done so if it did not believe that a confidential consulting relationship had existed with him.[339] However, at no time did counsel for AstraZeneca provide Dr. Moeckel with any form of nondisclosure or confidentiality agreement.[340] The PSC argues that no confidential information was disclosed at that meeting; rather, the PSC asserts, based on the declaration of AstraZeneca counsel, that Dr. Moeckel and AstraZeneca counsel discussed the following topics: Dr. Moeckel's professional background and research, medical literature, AstraZeneca's

[337] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. C [Legal Fee Schedule] No. 2:19-cv-00850, ECF No. 36-5; AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. D [hereinafter Consulting Agreement Between Dr. Gilbert Moeckel & IceMiller] No. 2:19-cv-00850, ECF No. 36-6.
[338] Oral Args. 31:3-24, 48:10-49:4, Apr. 4, 2022.
[339] Mem. of Law in Supp. of AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel 5-6. Declaration of Katherine Althoff 2.
[340] Oral Args. 42:11-14, Apr. 4, 2022.

scientific and medical theories, Dr. Moeckel's initial professional opinions, and other potential consulting experts.[341]

On January 30, 2017, AstraZeneca counsel sent Dr. Moeckel two binders containing medical literature about PPIs.[342] Dr. Moeckel testified that he never reviewed them.[343] Counsel for AstraZeneca asserts that 28 of the 30 articles contained in these binders were referenced in his expert report.[344]

AstraZeneca's counsel and Dr. Moeckel had no contact from January 2017 until November 2020. During this period, Dr. Moeckel did not submit any invoices, nor did he receive any payment from AstraZeneca's counsel.[345] When AstraZeneca's counsel contacted Dr. Moeckel in November 2020, he stated, "[u]nfortunately I am not available for legal consultation in the foreseeable future."[346]

Dr. Moeckel began working with Plaintiffs' counsel in late 2018, and his expert report was provided to Defendants in April 2021.[347] He was deposed in July

---

[341] PSC's Resp. to Mot. to Disqualify Moeckel 14-15 (citing Declaration of Katherine Althoff).
[342] Declaration of Katherine Althoff 3.
[343] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. B at 209:20-22 [hereinafter Moeckel Dep., July 7, 2021] No. 2:19-cv-00850, ECF No. 38-4.
[344] AstraZeneca's Br. in Resp. to Pls.' Opp'n to Defs.' Mot. to Disqualify Gilbert Moeckel 11 n.8, No. 2:19-cv-00850, ECF No. 49.
[345] *See* Moeckel Dep. 201:9-11, July 7, 2021; Oral Args. 33:22-24, Apr. 4, 2022.
[346] AstraZeneca's Mot. to Disqualify Dr. Gilbert Moeckel, Ex. H [Moeckel E-mail, Nov. 24, 2020] No. 2:19-cv-00850, ECF No. 36-16.
[347] *See* Moeckel Dep. 59:6-8, July 7, 2021; Oral Args. 39:19-20, Apr. 4, 2022 (Mr. Pennock: So it was in November of 2018 that we first started having contact with him.); Declaration of Katherine Althoff 3.

2021, at which time AstraZeneca's counsel first raised the issue of their earlier communications with him.

In the Third Circuit, in determining whether disqualification is appropriate, the court must make two determinations: (1) whether it was "objectively reasonable for the party seeking disqualification to have concluded that a confidential relationship existed with the expert[,]" and (2) whether the party seeking disqualification "disclose[d] any confidential information to the expert[.]"[348]

AstraZeneca argues that it had an objectively reasonable belief that it had retained Dr. Moeckel and shared confidential information with him at the January 2017 meeting and in its selection of materials it sent him thereafter. The PSC and Dr. Moeckel dispute these conclusions. Dr. Moeckel testified at his deposition that he did not believe he had been retained and that he never looked at the notebooks.[349]

In considering whether there was an objectively reasonable belief of retention, courts in the Third Circuit have considered: (1) the length of the relationship and the frequency of contact; (2) whether the moving party funded or directed the formation of the opinion to be offered at trial; (3) whether the parties entered into a formal confidentiality agreement; (4) whether the expert was retained to assist in the

[348] *See Fed. Trade Comm'n v. Innovative Designs, Inc.*, No. 16-1669, 2018 U.S. Dist. LEXIS 42510, at *16-17 (W.D. Pa. Mar 15, 2018); *see also In re Diet Drugs Prods. Liab. Litig.*, No. 07–20144, 2009 WL 1886131, at *3 (D.N.J. June 26, 2009).
[349] Moeckel Dep. 202:6-12, 209:20-22, July 7, 2021.

litigation; (5) whether the expert was paid a fee; and (6) whether the expert was asked to agree not to discuss with opposing parties or counsel.[350] The burden of proof rests on the party moving for disqualification.[351]

While there was undoubtedly sloppiness in documentation and communication by everyone involved, I conclude that, collectively, the facts here do not support an objectively reasonable belief that Dr. Moeckel was retained by AstraZeneca's counsel. First, there is no retention agreement signed by both parties. Dr. Moeckel sent AstraZeneca's counsel a fee schedule and a document that he signed that purported to be a "Consulting Agreement" in November 2016; however, AstraZeneca's counsel never signed it. Nor did AstraZeneca's counsel ever send Dr. Moeckel a standard retainer agreement, as is typical when counsel retain experts for litigation. Such retainer agreements typically contain confidentiality provisions, which Dr. Moeckel's one-page document did not, as well as terms relating to scope of work, payment amount and timing, and billing requirements. Dr. Moeckel's "consulting agreement" looks nothing like a typical expert retainer agreement. It does not appear to be different from his fee schedule other than the document's title.

---

[350] *Innovative Designs, Inc.*, 2018 U.S. Dist. LEXIS 42510, at *17-18 (quoting *Syngenta Seeds, Inc. v. Monsanto Co.*, No. 02-1331, 2004 U.S. Dist. LEXIS 19817, at *2 (D.N.J. Sept. 27, 2004)).

[351] *See, e.g.*, *Syngenta Seeds, Inc.*, No. 02-1331, 2004 U.S. Dist. LEXIS 19817, at *2 (D.N.J. Sept. 27, 2004) (declining to disqualify an expert witness when the moving party did not point to specific confidential information that it disclosed to the expert).

Second, Dr. Moeckel never submitted a bill nor received any compensation from AstraZeneca. Third, the nearly four-year period where there was absolutely no communication between Dr. Moeckel and AstraZeneca's counsel hardly supports a belief that they were working together. Finally, as noted above, there was no confidentiality agreement or other agreement spelling out with whom Dr. Moeckel could or could not communicate.

With regard to disclosure of confidential information, AstraZeneca states in its Motion that during the January 2017 meeting, "Ms. Althoff shared confidential case strategy with Dr. Moeckel and solicited his opinions on key defense arguments as well as on potential consulting experts."[352] However, as noted, AstraZeneca never provided a confidentiality or retention agreement to Dr. Moeckel at that meeting or any other time. It is somewhat incongruous now to assert an expectation that the discussion at that meeting was confidential when no effort at the time was made to memorialize that expectation in a legally binding document, as is commonplace when working with third parties in litigation. Moreover, Dr. Moeckel testified that the topics discussed at that meeting did not involve disclosure of confidential information.[353]

AstraZeneca also asserts that the selection of materials for the binders sent to Dr. Moeckel in January 2017 reflects attorney thought processes and thus are also

[352] AstraZeneca's Mem. to Disqualify Moeckel 12.
[353] Moeckel Dep. 204:7-209:22, July 7, 2021.

confidential information.[354] First, Dr. Moeckel testified that he never looked at these notebooks.[355] The fact that he submitted no bills to AstraZeneca for time spent reviewing them tends to support that testimony. Additionally, AstraZeneca has not presented any evidence that the materials included in the notebooks were not publicly available. The fact that 28 out of 30 of them were referenced in Dr. Moeckel's expert report, according to AstraZeneca, does not prove that he was using confidential information provided to him by AstraZeneca's counsel in his work for plaintiffs; it merely shows that what he was provided were materials relevant to the issues in this litigation.

The factual record does not support an "objectively reasonable" belief that Dr. Moeckel had been retained by AstraZeneca under the criteria utilized by courts in the Third Circuit. Accordingly, I recommend that AstraZeneca's motion to disqualify Dr. Moeckel be denied.

2. Motions to Exclude Dr. Moeckel

AstraZeneca and Takeda argue that Dr. Moeckel's testimony should be excluded under *Daubert* on the grounds that he is not qualified to give the proposed testimony, his methodology is not reliable, and his proposed testimony does not fit with the issues presented in these cases. For the reasons set forth below, I recommend that the motions to exclude Dr. Moeckel's expert testimony be denied.

---

[354] AstraZeneca's Mem. to Disqualify Moeckel 12.
[355] Moeckel Dep. 209:20-22, July 7, 2021.

a. Qualifications

Defendants' fundamental argument is that Dr. Moeckel is not qualified to give the proposed testimony because his primary expertise is in human, not animal, renal pathology.[356] While it is correct that his primary expertise is in human pathology, Dr. Moeckel has also conducted and reviewed animal pathology on multiple occasions throughout his lengthy career.

Dr. Moeckel's general qualifications are undoubtedly impressive. He is a Professor of Pathology at the Yale School of Medicine, where the University named a research laboratory after him.[357] He is board-certified in pathology and has over thirty years of medical experience. He has served as a peer reviewer for the National Science Foundation and the American Heart Association and is on the Editorial Board for several medical journals, including the Journal of the American Society of Nephrology, Nephrology Dialysis & Transplantation, and the Kidney International Scholarly Research Network.[358] He has authored over 100 reports and publications related to CKD.[359] Additionally, his deposition testimony makes clear

[356] AstraZeneca's Mem. to Exclude Moeckel 8; Takeda's Mem. to Exclude Moeckel 8.
[357] AstraZeneca's Mot. to Exclude Op. Test. from Dr. Moeckel, Ex. A, [hereinafter Moeckel Expert Report (AstraZeneca)] No. 2:19-cv-00850, ECF No. 35-3; Takeda's Mot. to Exclude Dr. Moeckel, Ex. B [hereinafter Moeckel Expert Report (Takeda)] No. 2:17-cv-06124, ECF No. 80-4.
[358] Moeckel Expert Report (AstraZeneca) 3; Moeckel Expert Report (Takeda) 4.
[359] Moeckel Expert Report (AstraZeneca) Ex. A 7, 9-10; Moeckel Expert Report (Takeda) Ex. A 7, 9-10.

that he has conducted and reviewed studies relating to renal toxicity in animals on multiple occasions throughout his career.[360] He has been a speaker on a number of topics involving renal toxicity in animals.[361]

The fact that Dr. Moeckel may not have precise expertise relating to beagle kidneys, as argued by AstraZeneca, does not render him unqualified to offer any opinions about preclinical animal studies conducted by the Defendants in the six Bellwether Trial Cases. Rather, the extent of his experience is an appropriate topic for cross-examination at trial. Likewise, Dr. Moeckel's opinions about the presence or absence of CPN in some of the rat studies differ from those of Defendants' experts. Because the Court's gatekeeping function extends only to the reliability of an expert's methodology, not the Court's opinion on the correctness of the expert's conclusions, the discrepancies between the opinions of Dr. Moeckel and Defendants' experts can be addressed through cross-examination at trial.

Third Circuit law makes clear that an expert need not be the best or most qualified to testify at trial.[362] It is quite possible that there are other experts who are

---

[360] *See* Moeckel Dep. 72:11-23, July 7, 2021 (testifying that he looked at hundreds upon hundreds of rat and mouse kidneys and is very familiar with their kidney pathologies).

[361] Moeckel Expert Report (AstraZeneca) Ex. A, at 7, 9-10 (Dr. Moeckel has given presentations on the protective effect of Citrate on renal phosphate crystal formations in rats, and the effect of dietary phosphate and dehydration of crystal formation in rats).

[362] *See Pineda*, 520 F.3d at 244 ("[I]t is an abuse of discretion to exclude testimony simply because the trial court does not deem the proposed expert to be the best

better able to address the animal studies and what they do or do not show. That, however, is not a basis for excluding entirely the testimony of an expert with robust credentials like Dr. Moeckel's.[363]

b. Reliability

Defendants challenge Dr. Moeckel's methodology of reviewing slides of animal kidneys, particularly that the slides were not blinded as to drug administration, he did not use a numerical grading system, he kept only "mental notes" and did not create a written record of his review process, and he only looked at certain studies, excluding ones that were "negative."[364] Essentially, they argue

---

qualified or because the proposed expert does not have the specialization that the court considers most appropriate." (citing *Holbrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 782 (3d Cir. 1996)).

[363] It also seems rather incongruous for AstraZeneca to argue on the one hand that Dr. Moeckel should be disqualified because of AstraZeneca's prior communications with him and expressed desire to have him work with them and on the other hand that he is not qualified to testify. Counsel at oral argument attempted to explain this apparent incongruity by asserting that it was their intent to have him testify only as to human pathology. Oral Args. 53:14-16, Apr. 4, 2022. But, since there is no retention agreement spelling out what he was to do, this cannot be confirmed. Furthermore, the materials provided to Dr. Moeckel by AstraZeneca included at least one animal study. Moeckel Expert Report (AstraZeneca) Ex. B; Moeckel Expert Report (Takeda) Ex. B.

[364] AstraZeneca's Reply in Supp. of Defs.' Mot. to Exclude Expert Test. of Dr. Gilbert Moeckel 7, No. 2:19-cv-00850, ECF No. 48 [hereinafter AstraZeneca's Reply Br. on Moeckel] (noting that Dr. Moeckel "specifically stated that he did not take any notes, other than 'mental notes,' and only took screenshots of the slides that looked interesting to him, not all 1,100 available slides"); Takeda's Mem. to Exclude Moeckel 2 (stating that "Dr. Moeckel simply selected a handful of slides that he knew were not in the animal studies control group, made 'mental notes,' and used

that Dr. Moeckel "cherry-picked" data that supported his conclusions and had no discernable methodology.[365]

Defendants have raised legitimate concerns about the objectivity and replicability of Dr. Moeckel's methodology. The question is whether his methodology is so unreliable as to warrant exclusion. While this is a close call, I recommend that the testimony be allowed, recognizing that these methodological issues can be raised during cross-examination to challenge his conclusions.

Defendants rely on *In re Diet Drugs*, which excluded an expert's proposed testimony that utilized a scientifically unreliable methodology.[366] In that case, the expert, Dr. Colin Bloor, visually observed pathology slides from a particular study and recorded narrative descriptions of what he saw in each. He organized those descriptions into verbal categories and then collapsed and converted the categories into numerical scores. Each step was done without reexamining the slides. Because the slides were not prepared in a manner that would best reveal heart structures, Dr. Bloor could only comment to a reasonable degree of medical

---

them in his report, discarding the thousands of other slides that did not support his conclusion.").

[365] AstraZeneca's Reply Br. on Moeckel 2 (arguing that Dr. Moeckel's methodology lacks scientific basis, and his report is premised upon cherry-picked data and litigation-driven, preformulated opinions); Takeda's Mem. to Exclude Moeckel 2.

[366] *See* AstraZeneca's Mem. to Exclude Moeckel 13 (citing *In re Diet Drugs Prods. Liab. Litig.*, No. 99-cv-20593, 2001 U.S. Dist. LEXIS 1174 (E.D. Pa. Feb. 1, 2001); Takeda's Mem. to Exclude Moeckel 13 (citing same).

certainty as to the myocardium of each rat's heart, not the valves that were the heart structure at issue in that case.[367]

The court in *In re Diet Drugs* emphasized the fact that Dr. Bloor's semi-quantitative scoring methodology had not been demonstrated to have a known or potential rate of error, was not shown to be replicable (because Dr. Bloor scored his recategorizations of the narrative descriptions and never actually assigned a numerical score to any of the slides), and did not have any control standards in place for application of the scoring system.[368]

Dr. Moeckel's methodology is distinguishable from Dr. Bloor's in *In re Diet Drugs*. As noted above, Dr. Moeckel's thirty years of experience in reviewing pathology and review of relevant literature informed his analysis. He states that he reviewed thousands of histopathology slides and compared his findings between dosed groups and control groups, males and females, and adults and neonatal animals.[369] He did not create a subjective numerical valuation of data as Dr. Bloor did. His purpose was to evaluate lesions identified by Defendants' pathologists in

[367] *In re Diet Drugs Prods. Liab. Litig.*, No. 99-cv-20593, 2001 U.S. Dist. LEXIS 1174, at *31 (E.D. Pa. Feb. 1, 2001).
[368] *Id.* at *37.
[369] Moeckel Expert Report (AstraZeneca) 7-8; Moeckel Expert Report (Takeda) 6-7.

their review of Defendants' preclinical studies and determine whether he concurred in their characterization.[370]

Dr. Moeckel's methodology is also distinguishable from that described in *Carnegie Mellon Univ. v. Hoffmann-LaRoche, Inc.*, also relied upon by Defendants.[371] In that case, the expert, who had a significant financial interest in the outcome of the litigation, departed from standard practices by reinterpreting published data without considering the quality of the data, experimental controls that refuted his opinion, and more probable explanations for the published results.[372] Unlike that expert, Dr. Moeckel states that he reviewed every slide in the forty studies provided to him by AstraZeneca and Takeda, documented his own pathological findings, and compared his findings to a large body of scientific literature and related materials, ultimately selecting a handful of studies to discuss in his expert reports.[373] Thus, Dr. Moeckel's methodology is "ground[ed] in the methods and procedures of science" and can be appropriately addressed on cross-examination.[374]

---

[370] *See* Moeckel Expert Report (AstraZeneca) 6; Moeckel Expert Report (Takeda) 5-6.
[371] AstraZeneca's Reply Br. on Moeckel 8 (citing *Carnegie Mellon Univ. v. Hoffmann-LaRoche, Inc.*, 55 F. Supp. 2d 1024, 1034 (N.D. Cal 1999)). Takeda's Mem. to Exclude Moeckel 13.
[372] *Carnegie Mellon Univ. v. Hoffmann-LaRoche, Inc.*, 55 F. Supp. 2d 1024, 1034 (N.D. Cal 1999).
[373] *See* Moeckel Expert Report (AstraZeneca) 4-8; Moeckel Expert Report (Takeda) 5-6.
[374] Daubert, 509 U.S. at 590.

The Third Circuit in *Paoli* held that to determine reliability, a court must look at the scientific validity of the methodology upon which the expert bases an opinion.[375] The expert must, at a minimum, identify the methodology or procedures used or explain how they reached their conclusions.[376] While Dr. Moeckel's description of his methodology is not perfect, its flaws can be addressed and highlighted for the jury through cross-examination. On balance, I do not believe the flaws pointed out by Defendants as to Dr. Moeckel's methodology rise to the level of its probative value being substantially outweighed by its prejudicial effect.[377]

c. Fit

The crux of Defendants' argument regarding lack of fit is that Dr. Moeckel's opinions about the presence of CPN versus acute tubular injuries in rat kidneys would not be helpful to a trier of fact in trying to make determinations about the presence or absence of data supporting a link between PPIs and CKD in humans.

Defendants' position seems to be that there is a lack of fit because (1) Dr. Moeckel is opining only about what he sees occurring in the dosed animal group in the preclinical studies, not about the ultimate issue of whether PPIs can cause CKD in humans, and (2) Dr. Moeckel's conclusions about those preclinical studies are that

[375] *Paoli*, 35 F.3d at 742.
[376] *See Sikkelee*, 522 F. Supp. 3d at 158; *see also Buzzerd*, 669 F. Supp. 2d at 514.
[377] *See Bruno*, 2015 U.S. Dist. LEXIS 156339, at *140 (internal quotation omitted).

the animals experienced acute tubular lesions (rather than CPN as AstraZeneca concluded) and that findings of acute lesions are irrelevant to discussions of CKD.

I recommend that these arguments be rejected for two reasons: First, Dr. Moeckel reviewed pathology from animals in preclinical studies submitted to FDA in support of the manufacturers' NDAs for these PPIs. Defendants may not agree with Dr. Moeckel's conclusions and can challenge them on cross-examination, but there is no dispute that animal studies provide FDA, the scientific community, and juries with important information about a drug's safety and efficacy. That Dr. Moeckel is not being offered to testify as to whether PPIs can cause acute or chronic injuries in humans, per the stipulation by the PSC, does not render his observations about these preclinical studies and their proper interpretation irrelevant.

Second, a key issue in this litigation is the relationship between a finding of AKI and CKD. Dr. Moeckel opines that some dosed animals experienced acute lesions in the preclinical studies and that these lesions were incorrectly identified by Defendants as CPN.[378] Defendants will have an opportunity to cross-examine Dr. Moeckel on the significance, if any, of these opinions to the issues in these cases. The fact that they involve acute injuries does not mean they do not fit with the issues

[378] Moeckel Expert Report (AstraZeneca) 26-27; Moeckel Expert Report (Takeda) 21.

in this case, in particular given Dr. Ross's testimony regarding untreated AKIs.[379]

In *Paoli*, the court noted that the standard for valid scientific connection to the pertinent inquiry is higher than bare relevance and must help the trier of fact understand the evidence.[380] Dr. Moeckel's work may not help the jury in making determinations about the presence or absence of a link between PPIs and CKD, but it may be helpful in understanding the nonclinical studies relied upon by Defendants.

V. CONCLUSION

For the reasons set forth herein, I recommend that the *Daubert* and related motions discussed in this Report and Recommendation be decided as set forth above.[381]

A proposed order is attached.

Respectfully submitted,

ELLEN REISMAN
Special Master

[379] *Compare* Moeckel Expert Report (AstraZeneca) 25-27, and Moeckel Expert Report (Takeda) 21, *with* Ross Expert Report 94.

[380] *See Paoli*, 35 F.3d at 743, 745; *Daubert*, 509 U.S. at 591 ("Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility.").

[381] To the extent the parties have raised in their briefing any arguments not expressly addressed in this R&R, I have considered them and recommend that they be rejected.